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CARDIAC ARREST*

Results of Attempted Cardiac Resuscitation in 42 Cases

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IN recent years the challenging problem of cardiac resuscitation has become increasingly important, and there is a need for better appreciation of the methods and indications for cardiac resuscitation. The purpose of this paper is to report our experience at the Grace-New Haven Community Hospital with cardiac resuscitation during a five-year period from December, 1948, to January, 1954. Major emphasis is placed on the need for prompt recognition of cardiac arrest and on the other hand, the futility of cardiac resuscitation when other conditions incompatible with life already exist.

The problem of an abrupt arrest of cardiac function is by no means confined to patients with heart disorders, or to those undergoing cardiac surgery. Though fortunately rare, the most tragic cases of cardiac arrest occur in children or in vigorous young adults undergoing relatively minor operative or diagnostic procedures; these patients in particular represent an absolute indication for a prompt attempt at cardiac resuscitation. Certainly every physician, in whatever field, should be familiar with this emergency and with the modern methods of resuscitation. Since speed of action is the most essential feature in successful resuscitation and preservation of normal brain tissue, it behooves every physician to formulate a plan for the treatment of cardiac arrest in the event that this catastrophe should occur in a patient under his care.

The term cardiac resuscitation applies to the action taken to save the life of a patient whose heart has suddenly ceased to beat, when there is reasonable expectation that with prompt treatment his normal cardiac and cerebral function can be restored for an indefinite period. The beating heart that stops abruptly may occasionally resume normal activity spontaneously (Fig. 1). A sharp blow on the anterior wall of the chest[1] or direct stimulation of the myocardium, as by a needle inserted through the chest wall, may be effective in restoring cardiac contractions.[2] Cardiac contractions may also resume in response to an electric stimulus applied to the chest wall[3] or to the region of the sinoatrial node.[4] Direct manual massage of the heart (Fig. 2), however, is generally regarded as the resuscitative measure of widest applicability and is especially indicated in conjunction with electric[5] or chemical[6] defibrillation in the presence of ventricular fibrillation.

For the purpose of this paper, the term "cardiac arrest" is used to include both cardiac standstill and ventricular fibrillation. A distinction between these two conditions is made where indicated, particularly in the method of resuscitation. So far as the present case material is concerned, cardiac resuscitation applies only to cases in which *cardiac massage* was actually carried out. Unless the right side of the chest was already open at the time of cardiac arrest, a left thoracotomy incision was employed. Cardiac massage was performed with the chest open in all but 4 cases, in which the heart was massaged from the abdominal cavity through the diaphragm.

FREQUENCY OF CARDIAC ARREST

During the five-year period included in this study, the diagnosis of cardiac arrest was made a total of 45 times in 44 patients (Table 1). In 1 of these patients cardiac function was restored spontaneously before any resuscitative measures were instituted after thirty-six seconds of arrest. In 2 others the heart was found to be beating when the chest was opened. In 41 patients resuscitative measures, including cardiac massage, were instituted, and in 1 cardiac resuscitation was attempted on two separate occasions, sixteen days apart. During the period of study cardiac arrest occurred in patients in the operating room approximately once for every 1900 operations performed. If, however, the 260 cardiac surgical procedures performed during the period covered by this report are excluded (there were 7 cardiac arrests in this group, giving a frequency of 1:37) the occurrence of cardiac

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arrest in all other types of surgery was about 1:3000. This rate is similar to that reported by Hinchey and Straehley[7] and others.[8,9]

Only 22 of the 42 attempts at cardiac resuscitation in this series were made on patients in the operating room. The 20 remaining attempts were made in a variety of locations (Table 2), most frequently in the patient's room.

Cardiac arrest occurred twice during approximately 470 cardiac catheterizations performed during the five-year period. One was a case of ventricular fibrillation in an adult with chronic congestive heart failure of undetermined cause (Case 12, Table 3 and Fig. 2); the other was cardiac standstill in a child with cyanotic congenital heart disease (Case 17, Table 3).

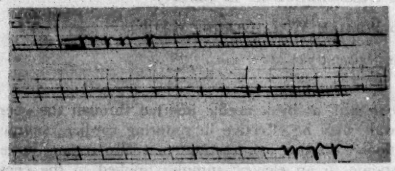

FIGURE 1. *Electrocardiogram, Showing Asystole of Approximately Thirty-six Seconds' Duration Followed by Spontaneous Resumption of Cardiac Contractions.*

ETIOLOGY

The major factors responsible for suddenly occurring cardiac arrest in this series are vagal stimulation, anoxia and hypercapnia, direct stimulation of the heart, and drug sensitivity. It must be realized that in many cases sudden cardiac arrest in a normal heart is probably preventable, and if a similar catastrophe is to be avoided in the future, every effort should be made to determine the etiologic factors involved in every case. To this end, it is essential that all facts concerning the cardiac arrest — particularly those immediately preceding it — be carefully recorded by the operator as soon as possible. The most likely primary causes for cardiac arrest in our cases are listed in Table 4. The contributing causes and other pertinent data are assembled in Table 3.

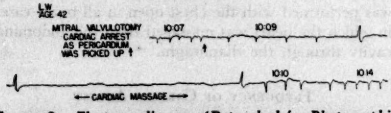

FIGURE 2. *Electrocardiogram (Retouched for Photographic Purposes) in Case 1, Showing Bradycardia, Ectopic Beats and Asystole As the Pericardium Was Picked up at Operation; Rapid Resumption of Cardiac Activity Followed Cardiac Massage.*

In 2 cases electrocardiograms providing a complete record of the episode of cardiac arrest (Fig. 1 and 2) were obtained. In 1 other case arrest occurred during cardiac catheterization at a time when pressures were being recorded from the right atrium. An electrocardiographic tracing was begun immediately thereafter (Fig. 3). In these 3 cases especially, and in some others, the exact time of cardiac arrest and the progression of events at that time are known, and certain reasonable deductions about causation can be made. In a number of other cases it was impossible to assign a definite cause, since many important facts relating to the previous events, surgical manipulations, conduct of anesthesia and so forth were not known. It is probable that, in many cases listed as "unknown or uncertain," cardiac arrest was secondary to vagal reflexes. Although difficult to prove in an individual case, vagal-reflex inhibition of impulse formation at the sinoatrial node has recently been emphasized as the single most important etiologic factor in cardiac standstill.[10,11] The importance of hypoxia and especially hypercapnia in potentiating the vagal effect on the pacemaker has also been demonstrated.[12] Intubation, extubation and suctioning of the trachea have been suggested as important precipitating causes of cardiac arrest, probably mediated, at least in part, by vagal reflexes.[13] Direct stimulation of the vagus nerve or its branches during surgery may initiate marked bradycardia or cardiac arrest, as demonstrated by 4 cases in this series.

TABLE 1. *Cardiac Resuscitation.*

TYPE OF CASE	NO. OF CASES
Abrupt cardiac arrest diagnosed	45
Total patients	44
Error in diagnosis	2
Spontaneous return of cardiac action	1

DIAGNOSIS

It has been principally the anesthetists and the nurses who have had first opportunity to appreciate the possibility of cardiac arrest in the patients of this series, since 32 of the 42 cases occurred either in the operating room or in the patient's room. To make or confirm the diagnosis clinically, the physician attempting resuscitation has relied on the absence of the pulse, respirations, blood pressure and heart sounds. Few situations in medicine require the accurate but rapid diagnosis, the careful judgment of indications and immediate exercise of the correct and effective therapy demanded of the physician suddenly

TABLE 2. *Place of Arrest.*

PLACE	NO. OF CASES
Operating room	22
Patient's room	10
Ambulance (before arrival)	3
Emergency room	2
Cardiac-catheterization room	2
X-ray room	1
Constant-temperature room	1
Recovery room	1

faced with a cardiac arrest. It might be expected under the circumstances that mistakes in diagnosis would be common. Actually, in this series, there was a question of diagnostic errors in only 2 cases. In these the diagnosis of cardiac arrest was made clinically on what appeared to be completely justifiable grounds, but when the heart was visualized it was seen to be beating. There is a question in each of these cases whether there was a mistake in diagnosis, a spontaneous resumption of cardiac activity or a resumption of cardiac activity owing to the stimulus of thoracotomy. In 1 of these 2 patients an incision in the skin had been begun during an elective thoracotomy on the left at the time cardiac arrest was suspected by the anesthetist. The thoracotomy opening was rapidly completed, and the heart was found to be beating slowly and feebly. Rapid recovery of normal cardiac function followed adequate oxygenation and cardiac massage. In the second case, when cardiac arrest was suspected, an unsterile emergency thoracotomy was performed in the outpatient clinic where the patient was undergoing local anesthetization with tetracaine (Pontocaine) for bronchography. The heart was found to be contracting slowly on exposure. This patient also recovered completely, with no apparent ill effects from the thoracotomy. Without proof of cardiac arrest these cases are considered as mistakes in diagnosis and are omitted from the statistics concerning results of treatment. In all other cases in this series the diagnosis was proved by visualization or palpation of the heart.

The diagnosis of cardiac arrest is incomplete without some estimation of the time elapsed since the heart ceased to beat, since this is an important factor in the decision to attempt resuscitation. In several of the patients in this series who were unattended or who had not reached the hospital at the time cardiac arrest began, knowledge of the time elapsed would probably have precluded any attempt at resuscitation.

Treatment

In this series direct cardiac massage was the major therapeutic tool in each case. The procedure was usually carried out through a thoracotomy on the left; the pericardium was opened only when necessary to perform more adequate massage or to defibrillate the ventricles. One successful resuscitation (Case 2, Table 3) was carried out through the right side of the chest, and in 2 other hearts (Cases 6 and 7, Table 3) cardiac function was restored by transdiaphragmatic massage through an abdominal wound. In at least 1 patient (Case 16, Table 3), massage was apparently delayed while epinephrine was injected into the heart through the unopened chest as a resuscitative measure. When it became evident that this was ineffective, thoracotomy and massage were initiated. Cardiac function was restored after a short period of massage but there was no evidence of returning cerebral function by the time of death twenty-six hours later.

Cardiac arrest occurred in 8 patients undergoing operations on the heart, great vessels or lungs. Although the heart was under direct vision and resuscitative measures, including cardiac massage, were promptly begun, completely successful resuscitation was obtained in only 2 of these patients. It is to be noted, however, that all but 1 patient in this group had severe disease or malformation of the heart.

When standstill occurred outside the operating room, cardiac massage was undertaken by the first surgeon to see the patient while others began artificial respiration and performed the other necessary functions (Table 5). The simplest equipment has been kept on the wards for these purposes. A sterile knife and pharyngeal airway are stored together in a large test tube. Sterile gloves and an emergency oxygen tank with a face mask and an inflatable rubber bag attached are likewise readily available on each ward. Several large kits of instruments similar to those described by Leeds[14] are wrapped in bright-red drapes to identify them easily as "cardiac-arrest kits." These kits have been kept at critical points — the operating suites, the cardiac-catheterization room and the room of the last patient to undergo cardiac surgery. They have been used to initiate thoracotomy and massage when immediately available, but frequently the set has arrived after massage has already been started by means of simpler and more readily available equipment. The rib spreader contained in the large kit has been very useful in preventing painful constriction of the operator's wrist between the patient's ribs during cardiac massage. The kit has also been of great value in closing the chest incision under sterile conditions after the resumption of heart action.

No serious difficulties were encountered as a result of opening the chest outside the operating room. The use of a pharyngeal airway and close-fitting face mask, with intermittent positive-pressure inflation of the lungs by manual compression of the attached rubber bag, gave apparently adequate ventilation. Mouth-to-mouth or mouth-to-mask breathing with the tongue pulled forward has been shown to be quite effective as a means of artificial respiration,[15] but was necessary on only 1 occasion in this series. Generally, the passage of an endotracheal tube took too long. This, together with the possibility of the initiation of undesirable vagal reflexes by intubation, led to abandonment of the endotracheal tube in this situation unless it was already in place at the time of arrest.

An outline of the basic principles in treatment of cardiac arrest appears in Figure 4, copies of which hang above the scrub sinks in the operating suites of the Grace-New Haven Hospital as constant reminders for the surgical and anesthesia staffs. Other copies are posted in the cardiac-catheterization room and the emergency room.

Ventricular fibrillation occurred in this series as a primary arrhythmia only once (Case 12, Table 3)

TABLE 3. *Summary of Attempted Cardiac Resuscitation.*

CASE NO.	AGE	PRIMARY DIAGNOSIS	HOSPITAL SERVICE	PRINCIPAL CAUSE OF ARREST	CONTRIBUTING CAUSES	TIME OF ARREST	SURVIVAL TIME*
	yr.						
Group 1 (Complete Recovery):							
1	42	Mitral & aortic stenosis	Cardiovascular	Vagal reflex	Continued stimulation in presence of bradycardia	Traction on pericardium	
2	1	Tetralogy of Fallot	Cardiovascular	Vagal stimulation	Anoxia (?cyclopropane)	Traction on vagus during Blalock anastomosis	
3	37	Mitral & aortic stenosis	Cardiovascular	Unknown	Uncorrected aortic stenosis; quinidine.	4 days after mitral valvulotomy	
4	48	Mitral stenosis & insufficiency	Cardiovascular	Unknown	Uncorrected mitral stenosis; large atrial thrombus; ?quinidine.	24 hr. after exploratory thoracotomy	
5	55	Causalgia (right index finger)	Cardiovascular	Drug idiosyncrasy		10 min. after dorsal sympathetic nerve block with Xylocaine	
6	70	Bleeding peptic ulcer	General	Anoxia	Hemorrhage; thiopental; cyclopropane; tetracaine.	Just prior to incision for emergency laparotomy.	
7	27	Intestinal obstruction	General	Drug idiosyncrasy		15 min. after procaine & tetracaine spinal anesthesia, during laparotomy incision	
Group 2 (Temporary Recovery or Recovery of Heart Action Only):							
8	7	Croup	Pediatric	Anoxia (?reflex)	Acute laryngotracheitis; pneumothorax; atelectasis.	Just after clearing of blocked tracheotomy tube	32 hr.
9	18	Pulmonary tuberculosis	Thoracic	Anoxia	Hemorrhage; ventricular fibrillation; cyclopropane.	During difficult hilar dissection	2 hr.
10	3	Croup	Pediatric	Anoxia	Blocked airway	During clearing of tracheotomy tube	4 hr.
11	4	Tetralogy of Fallot	Cardiovascular	Vagal stimulation	anoxia; mongolism.	Traction on vagus during Blalock anastomosis	4 hr.
12	46	Congestive heart failure	Medical	Mechanical stimulation	Irritable heart; ventricular fibrillation.	During cardiac catheterization	20 hr.
13†	62	Carcinoma of lung	Thoracic	Anoxia	Advanced disease; respiratory depression.	Before bronchoscopy after possibly excessive preanesthetic medication	36 hr.
14	3	Colostomy for perineal burns	General	Unknown	Varying depth of anesthesia for wound closure; open drop ether.	During closure of skin	6 hr.
15	50	Causalgia	General	Anoxia	Hemorrhage	During lumbar sympathectomy	24 hr.
16	24	Pelvic inflammatory disease	Gynecologic	Unknown	Varying depth of anesthesia (nitrous oxide & oxygen)	During closure of skin after hysterectomy	26 hr.
17	1	Cyanotic congenital heart disease	Pediatric	Mechanical stimulation	Anoxia; supplementary anesthesia (thiopental).	During cardiac catheterization	6 hr.
18	23	Pelvic inflammatory disease	Gynecologic	Unknown	?Anoxia (?reflex)	During hysterectomy	8 mo.
19†	82	Recurrent carcinoma of neck	General	Unknown	Prolonged surgery; poor general condition; ?transfusion reaction.	At end of radical neck dissection	3 hr.
20	34	Acute urinary retention	Urologic	Anoxia	?Blocked airway (vomiting & aspiration); ?pulmonary embolus; ?potassium intoxication (nonprotein nitrogen of 168 mg. per 100 cc. & potassium of 6.8 milliequiv. per liter); ventricular fibrillation.	6 days after cystostomy	5 hr.

TABLE 3 *(Concluded).*

CASE NO.	AGE	PRIMARY DIAGNOSIS	HOSPITAL SERVICE	PRINCIPAL CAUSE OF ARREST	CONTRIBUTING CAUSES	TIME OF ARREST	SURVIVAL TIME*
	yr.						
21	2	Incarcerated inguinal hernia	General	Anoxia	Excessive anesthesia (open drop ether)	During hernia repair	48 hr.
22†	80	Fracture of femur	Orthopedic	Anoxia	Blocked airway (?reflex—tracheal suction)	During hip-nailing procedure patient vomited & aspirated	1 hr.
23	½	Extrophy of bladder	Urologic	Anoxia	Blocked airway (?reflex—tracheal suction)	During repair of wound dehiscence patient vomited & aspirated	45 min.
Group 3 (Complete Failure to Restore Heart Action):							
24	38	Mitral stenosis	Cardiovascular	Arrhythmia	Intermittent atrial fibrillation throughout operation; severe congestive heart failure.	Chest closure after mitral valvulotomy	
25	4	Subgaleal abscess	Neurologic	Unknown	?Deepened anesthesia (?reflex)	Immediately after supplementary thiopental intravenously for incision & drainage	
26†	67	Carcinoma of breast	General	?Acute adrenal insufficiency	Bilateral adrenalectomy	After abdominal closure after bilateral adrenalectomy	
27	41	Mitral stenosis	Cardiovascular	Anoxia	Hemorrhage; severe heart disease.	Immediately after mitral valvulotomy	
28‡	37	Aortic stenosis after mitral valvulotomy	Cardiovascular	?Arrhythmia, secondary to aortic stenosis	Overdigitalization; congestive heart failure; aortic stenosis.	16 days after successful resuscitation from 1st arrest	
29	3	Tetralogy of Fallot	Cardiovascular	Vagal stimulation	Anoxia; ?cyclopropane.	Traction on vagus during Blalock anastomosis	
30†	65	Hypertensive & arteriosclerotic cardiovascular disease	Cardiovascular	Unknown	Coronary insufficiency; polycythemia vera; ?cyclopropane; episode of hypotension & bradycardia before arrest.	During lumbar sympathectomy	
31	69	Gastrointestinal hemorrhage	General	Anoxia	Hemorrhage; coronary insufficiency; angina; ?cyclopropane.	During skin incision for emergency laparotomy	
32†	66	Diaphragmatic hernia; atelectasis.	Thoracic	Myocardial infarction		Just after admission to hospital in x-ray room	
33†	88	Hip fracture	Orthopedic	Anoxia	Respiratory failure; hypertensive & arteriosclerotic heart disease; hypotension; spinal anesthesia, ?high level.	Before hip nailing	
34	About 30	Electrocution	Emergency	Electrocution		Diagnosis on arrival	
35†	18	Severe head injury	Emergency	Head injury		Pulse ceased in ambulance just before arrival	
36†	About 40	Gunshot wound of head	Emergency	Head injury		Diagnosis on arrival	
37†	50	Aortic stenosis	Cardiovascular	Arrhythmia	?Anxiety state	Several days before anticipated surgery	
38	½	Cyanotic congenital heart disease	Cardiovascular	Vagal stimulation	Anoxia	Traction on vagus during Blalock anastomosis	
39†	74	Carcinoma of rectum	General	?Stokes–Adams attack	Stokes–Adams attacks in history	12 days after abdominoperineal resection	
40†	49	Retroperitoneal lymphoma	General	Unknown	Carcinomatosis; ventricular fibrillation.	4 days after laparotomy	
41	28	Primary pulmonary hypertension	Cardiovascular	Unknown; ?arrhythmia.	Exploratory pericardiotomy	9 hr. after operation	
42	About 55	Carcinoma of colon	General	Unknown		Immediately after colectomy in recovery room	

*Group 2 only.
†In retrospect cardiac massage probably not indicated.
‡Same patient as Case 3 (see text).

although it developed during resuscitative measures for cardiac standstill a number of times. Although the ventricles almost always could be defibrillated by electric shock, no patient with ventricular fibrillation survived. This experience does not discourage our use of electric defibrillation of the ventricles, for there is ample experimental[8] and clinical[9] evidence of its efficacy if this treatment is applied early to the ventricle with good tone and fine fibrillatory movements. In some other reported series[9] an appreciable percentage of patients with ventricular fibrillation were successfully resuscitated. Before defibrillation, the injection of calcium chloride into the right or left ventricular chamber, followed by rapid massage, has usually provided improved myocardial tone and faster fibrillatory movements. Under the latter circumstances, defibrillation of the ventricles by a single shock of 110 volts for 0.1 to 0.2 second may be adequate to bring about cardiac arrest. Rapidly repeated shocks of 0.1 to 0.2 second may in some cases be more effective.[5] In very large hearts higher voltages may be required for defibrillation of the ventricles. The danger of electric burn of the myocardium is real and, according to recent experimental work,[16] increases with the number of shocks used. Therefore, in the present state of knowledge, it is probably advisable to employ defibrillating equipment that will allow the use of up to 220 or 270 volts if a single shock of 110 volts is not effective. The defibrillator described by Kouwenhoven and Kay[17] is probably the safest for the surgeon and the most efficient for the patient and can be slightly modified to provide any desired range of voltage. A smaller defibrillator, easily portable but without the safety factor of an isolation transformer, is advantageous and has been employed in some of the cases in this series.[18]

TABLE 4. *Primary Causes of Cardiac Arrest.*

CAUSE	NO. OF CASES
Vagal stimulation:	
Direct	4
Reflex	1
Anoxia:	
Hemorrhage	5
Blocked airway	5
Anesthesia	2
Head injury	2
Coronary occlusion	1
Sedation	1
Drug idiosyncrasy	2
Direct endocardial stimulation	
Cardiac catheterization	2
Primary arrhythmia	3
Acute adrenal insufficiency	1
Electrocution	1
Unknown or uncertain	12
Total	42

The ventricles arrested from fibrillation by electric shock may start to beat spontaneously, or it may be necessary to institute massage. Frequently, the defibrillated heart will fibrillate a second or third time, either during or soon after massage. The decision when and how much to massage the partially resuscitated heart presents a problem in clinical judgment.

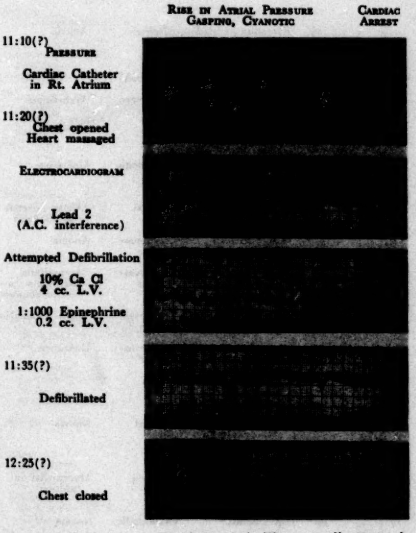

FIGURE 3. *Pressure Tracings and Electrocardiograms in Case 12 (A.A., a Forty-Six-Year-Old Man with Right-Sided Heart Failure).*

Ventricular fibrillation developed during cardiac catheterization.

Generally speaking, we have found that if the heart beat is reasonably forceful and rapid (more than 50 beats per minute), recovery of the heart will be progressive. Manipulation of the heart at this point in an effort to improve its action may precipitate another episode of arrest or fibrillation.

TABLE 5. *Status of Operator Performing Cardiac Resuscitation.*

CLASSIFICATION	NO. OF RESUSCITATIONS ATTEMPTED		
	SUCCESS	PARTIAL SUCCESS	FAILURE
Attending surgeon	4	9	5
Resident surgeon	1	3	4
Surgical house officer	2	4	8

In addition to cardiac massage and defibrillation when indicated, certain drugs have frequently been used in the treatment of cardiac arrest. Atropine was

administered intravenously in the management of significant bradycardias at operation. This drug has been effective in many patients in correcting what appeared to be dangerous bradycardias.

Calcium chloride in a 10 per cent solution was of principal value in the heart just before arrest, just after resuscitation or in ventricular fibrillation in which the movements were slow and coarse; 2 to 4 cc. was injected into the right or left ventricle and massaged if necessary into the coronary circulation. The response, especially after the first injection, was usually dramatic, with great improvement in cardiac tone and contractions. When combined with massage it was useful in improving the tone of the fibrillating heart. It must be given with caution in the very irritable heart or after vasopressor drugs, since it may precipitate fibrillation.

Vasopressor drugs include epinephrine, phenylephrine hydrochloride (Neo-Synephrine) and levarterenol bitartrate (Levophed). Epinephrine was occasionally given intravenously, but more often in cardiac arrest it was injected (1 to 2 cc. of 1:10,000 solution) directly into the *cavity* of the left or right ventricle. Caution should be exercised in the administration of this drug since it is likely to precipitate ventricular fibrillation, especially if used in large doses or if the injection is made into the muscular *wall* of the ventricle. It is indicated if there is little or no response to cardiac massage, calcium chloride or temporary clamping of the descending aorta. A suitable dilution

CARDIAC ARREST

RULES:

1. Waste no time — massage of heart must be started within 3 to 5 minutes of onset of arrest.
2. Open chest — 4th interspace.
3. Massage heart — 60-100 times per minute.
4. Establish airway and give oxygen at once.
5. Inject 10% calcium chloride — 2 to 4 cc. into cavity of right or left ventricle.

1. *ASSUME CARDIAC ARREST* if no blood pressure, no pulse and no heart sounds are obtainable.
2. *DO not delay* opening of chest for any reason after arrest occurs. Massage through chest incision is best. Open pericardium when necessary for adequate massage or for defibrillation. Use right chest incision if left not accessible.
3. Massage must be continued until vigorous contractions restored.
4. Adequate oxygenation is of utmost importance:
   a. Pull tongue forward.
   b. Insert pharyngeal airway.
   c. Oxygen mask with intermittent positive pressure.
5. If heart does not respond to above measures, repeat calcium chloride. Inject 0.1 to 0.2 cc. of epinephrine and 1 mg. of atropine into cavity (not wall) of left or right ventricle. Larger amounts, given as single dose, may cause fibrillation.

Call for Cardiac Resuscitation Kit (Instruments and drugs in Farnam and Private Operating Room) if sufficient equipment not available (a knife is the only absolute essential). Kit is wrapped in RED cloth.

If this is *your* patient (Surgeon, Anesthetist, Medic) *you* must institute cardiac massage unless more competent help is precisely at hand.

AS TIME FLIES THE NEURON DIES

FIGURE 4. *Chart Displayed in Operating Rooms, Describing Treatment of Cardiac Arrest.*

of levarterenol bitartrate is 4 cc. per 500 cc. of 5 per cent dextrose in water. Rarely is it necessary to exceed 20 drops of this dilution per minute intravenously, and caution must be exercised in treatment of the irritable heart not to speed the infusion, since ventricular fibrillation may be precipitated. This drug should be used early if there is not a prompt response to massage, calcium chloride and atropine.

In some of the early cases of this series, procaine either was given intravenously or was injected directly into the heart in many cases. During the more recent experience with cardiac arrest, however, this drug and its derivative, procaine amide (Pronestyl), have been given only when there was a definite indication of myocardial hyperirritability, since it is our impression that the arrested heart with normal irritability may be resuscitated more easily than one rendered unresponsive by these drugs.

Temporary clamping of the aorta just distal to the left subclavian branch was used in several cases in this series but was of benefit in only 1 patient. This measure is useful to increase the coronary and cerebral blood flow in laboratory animals, and it might have been of more aid in resuscitation of the human heart in some cases if it had been employed earlier.[19]

TABLE 6. *Results of Cardiac Massage.*

RESULT	NO. OF CASES
Complete recovery	7(16.7%)
Cardiac function alone restored	16(38.1%)
Failure	19(45.2%)
Total	42

Intravenous infusions of whole blood and electrolyte solutions were used in many cases. It is probable that in the presence of hypotension occasionally excessive amounts of these fluids were administered in an effort to improve the circulation, resulting in pulmonary edema. In a few cases, intra-arterial transfusions were given. The principal indication for this therapy appears to be severe hemorrhage when blood volume must be restored very rapidly.

RESULTS

The results of cardiac massage performed 42 times in 41 patients seen over a five-year period at the Grace-New Haven Hospital are recorded in Table 6. In Table 3 these cases were divided into three groups, depending on the therapeutic result. In Group 1 (survivors) one might assume that massage was definitely indicated in these 7 cases since recovery after cardiac resuscitation was complete. Four of these successful resuscitations were performed in the operating room, 2 in the patient's room and 1 in the constant-temperature room. Both patients who were successfully resuscitated in their rooms were accompanied only by members of the family at the time of cardiac arrest (Cases 3 and 5, Table 3). The revival of these patients was directly due to the speed with which the situation was recognized and brought to the physician's attention by the nurse who was summoned to the room. Another case of cardiac arrest with successful resuscitation occurred ten minutes after a Xylocaine injection for a dorsal sympathetic

nerve block in the constant-temperature room (Case 6, Table 3). Rapid response to a call from the anesthetist who recognized the arrest enabled this patient to survive. Two of the remaining 4 successfully resuscitated patients (Cases 1 and 2, Table 3) were undergoing cardiovascular operations with the heart under direct view by the surgeon so that no time was lost in appreciating the cardiac arrest or in beginning cardiac massage. In the other 2 cases (Cases 4 and 7, Table 3) the skin was being prepared before exploratory laparotomy for gastrointestinal hemorrhage and intestinal obstruction respectively, when cardiac arrest was suspected by the anesthetist. In these cases, incision into the abdomen was rapidly completed, and the heart massaged through the diaphragm. Ordinarily, we prefer the thoracotomy approach since more effective massage can be carried out through the chest.

TABLE 7. *Approximate Duration of Cardiac Arrest at the Time Resuscitation Was Begun.*

DURATION	FAILURE	CARDIAC FUNCTION ALONE RESTORED	COMPLETE SUCCESS
	NO. OF CASES	NO. OF CASES	NO. OF CASES
min.			
Less than 1	5	2	2
2-4	3	3	1
4-6	2	6	2
6-9	3	2	1
10 or more	—	1	—
Unknown	6	2	1
Totals	19	16	7

Of the 7 successfully resuscitated patients only 2 are alive at the present time (Cases 2 and 7, Table 3). Of the 5 others, 1 (Case 3, Table 3) died with a second cardiac arrest after sixteen days (Case 28, Table 3). Two died of their primary disease (Cases 1 and 5, Table 3) after thirteen and seven months, respectively. The remaining patients (Cases 4 and 6, Table 3) died of conditions unrelated to their original primary disease after six and eighteen months, respectively.

In Group 2 (Cases 8 through 23, Table 3) no patient fully recovered, but we believe, in retrospect, that cardiac massage was indicated in all but 1 (Case 13, with advanced carcinoma of the lung). In 2 others (Cases 19 and 22) massage was probably not indicated on the basis of age (over eighty).

In Group 3 there were 19 cases in which heart action could not be restored after cardiac massage. It is interesting that the average age of the patients in this group was forty-five years, as compared with thirty-three years in Group 2 and forty years in Group 1. There were in Group 3, as one might have expected, a larger number of cases in which, in retrospect, cardiac massage did not seem to be indicated. This was probably true in 9 of the 19 cases in this group. Two of these were patients with advanced malignant lesions (Cases 40 and 26, Table 3); 1 was a patient with Stokes–Adams attacks (Case 39, Table 3, in which the external electric stimulator might have been effective); 1 was over eighty (Case 33, Table 3); 2 had irreparable brain injuries (Cases 35 and 36, Table 3); and 3 had severe heart disease (Cases 30, 32 and 37, Table 3).

In about 50 per cent of the last group, however, resuscitation was believed both at the time and in retrospect to be indicated. The complete failure to resuscitate some of these hearts is not clearly understood.

DISCUSSION

The obvious and regrettable fact is that many of these cases of cardiac arrest occurred in young patients and might have been avoided. Cardiac arrest having occurred, however, precious time was sometimes lost in diagnosis and in the institution of cardiac massage. Even though the hearts of many of the patients in this series were resuscitated for a time, cerebral damage had most probably taken place by the time circulation of blood was restored. If the heart had continued to function for a longer time some cerebral function might have returned in some patients, but the evidence suggests that significant cerebral damage was a major cause of failure in cardiac resuscitation in these cases. This suggests that in the cases in Groups 2 and 3, in which massage was believed to be indicated, cardiac resuscitation might have been more effective if it had been begun sooner after the occurrence of arrest (Table 7). The truly emergency nature of cardiac arrest must be appreciated if a successful resuscitation is to be hoped for. Nevertheless, a short but definite time (*one minute*) should be spent in confirmation of the diagnosis and in consideration of the indications for resuscitation in a particular patient. A certain diagnosis of cardiac arrest cannot always be made unless the heart is in view or an electrocardiogram is being recorded. Time is so precious under these circumstances that if a smart blow on the anterior wall of the chest does not restore cardiac action, thoracotomy and cardiac massage should be promptly performed with a diagnosis of *probable cardiac arrest*.

An attempt at cardiac resuscitation is indicated when it is expected that cardiac and cerebral function normal for that patient will return. Unquestionably, a conflict of opinion regarding the wisdom of attempted resuscitation in the presence of a serious underlying disease or condition will arise from time to time. Unfortunately, the state of the disease or condition and its prognosis may not be known at the time of cardiac arrest. Whether resuscitation will be attempted under these circumstances must always depend on the judgment of the physician in attendance at the time. We believe that attempts at resuscitation are probably not worth while if not begun be-

fore ten minutes of arrest have elapsed, in a patient not subjected to hypothermia, since major irreversible anoxic damage to the brain will have occurred in most patients.

It is the ultimate aim of this and similar studies to provide a basis for the prevention and more effective treatment of the dread complication of cardiac arrest. We believe that accounts of all attempts at resuscitation should be collected and reported so that this condition can be widely appreciated and understood. The difficulty encountered in resuscitation of the arrested heart points clearly to the need for a better understanding of methods for the prevention of this catastrophe. The following preventive measures should be considered when applicable before, during and after any operative or diagnostic procedure:

Adequate oxygenation and ventilation.

Close observation of changes in cardiac rate or rhythm; withdrawal of all stimuli in the presence of rapid runs of ectopic ventricular beats or bradycardia.

Preoperative vagal inhibition with atropine; repetition during operation as indicated.

Repression of myocardial response to local stimuli in selected cases.

Gentle manipulations during *all surgery*, particularly in the region of the heart and great vessels.

Drug sensitivity: careful testing for sensitivity, with adequate sedation.

Careful cardiac stimulation in the presence of an acutely failing circulation (by means of levarterenol bitartrate and calcium chloride).

Careful evaluation and treatment of cardiac disorders.

Constant reminders to the staff of the causes, methods of prevention and treatment of cardiac arrest.

Summary and Conclusions

Abrupt cardiac arrest was diagnosed 45 times over a five-year period in the Grace-New Haven Community Hospital. In 2 patients the heart was beating when the chest was opened, and in 1 other, the heart resumed activity spontaneously. These 3 patients recovered uneventfully. Resuscitation by cardiac massage and other supportive measures was attempted 42 times. There were 7 (16.7 per cent) successful resuscitations, with return of normal cardiac and cerebral function. Sixteen (38.1 per cent) patients were partially resuscitated and had temporary return of cardiac activity and partial cerebral function for forty-five minutes to about eight months. There were 19 (45.2 per cent) cases in which no cardiac function could be restored. In retrospect cardiac massage would probably not have been considered indicated, owing to the presence of an underlying lethal condition, in 12 of the 35 unsuccessful cases.

The major causes of failure appeared to be a delay in the recognition of cardiac arrest and in the institution of cardiac massage. Also, the presence of a serious though not necessarily fatal underlying disease or condition seemed to have seriously compromised a number of attempts at resuscitation. The treatment of cardiac arrest is clearly deficient at present, and the greatest hope for progress lies in prevention of its occurrence.

We are indebted to the physicians and surgeons who generously permitted us to report cases from their private services.

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PRIMARY PROSTHESIS FOR SUBCAPITAL FRACTURES OF THE NECK OF THE FEMUR

Preliminary Report

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THE determining factors in the treatment of a patient with a fracture of the neck of the femur are the age and general condition of the patient and the level of the fracture. A fracture at a very high level offers a much poorer prognosis than one located at the middle or at the base of the neck. In true subcapital types a realistic appraisal may lead the surgeon to anticipate such poor results from the standard nailing operation that he is tempted to apply a replacement prosthesis as a primary procedure. The present article offers a study of 51 consecutive cases so treated in private practice. Only special cases, in which the type of fracture seemed to preclude success by routine nailing, were selected for this treatment.

The rationale for such treatments is based on four maxims of hip surgery. First, it is conceded that the result of a successful hip-nailing operation is better than that of any substitution prosthesis. But, secondly, as has been stated, subcapital fractures in aged persons offer extremely unfavorable prospects of success from nailing. Thirdly, an essential requirement after nailing of these high fractures is to continue full immobilization of the patient until strong fibrous union or early bony callus has developed—a period of not less than four and preferably six to eight weeks. Finally, the necessity for prolonged bed rest defeats the prime objective of treatment of the aged, which is early ambulation. Even after every precaution has been taken a subcapital fracture may break down with nonunion, requiring a subsequent reconstruction operation. Obviously, the aged can ill afford the double jeopardy of prolonged disability followed by later surgery.

As against these hazards and uncertainties, the primary use of a prosthesis in subcapital fractures offers many advantages. For example, it allows almost immediate ambulation. Even light weight bearing, assisted by crutches, can be permitted very early. The cost of treatment is thus materially reduced if patients are enabled to leave the hospital relatively soon after operation. Convalescence can be carried out at home without the need of elaborate physiotherapy. The fear of late complications from nonunion or necrosis of the head is eliminated.

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SELECTION OF CASES

Our own experience in the use of prostheses generally is by no means free from complications or failures. However, we have come to regard this as a very promising form of treatment once its difficulties are fully understood.[1] In reporting on the present series of cases, we wish to emphasize the particular phases of treatment that deserve special consideration. To begin with, the proper selection of cases is of great importance. Obviously, it would be fruitless to insert a prosthesis in anyone who will never walk again because of general debility, nor should it be considered in a patient who is moribund or unfit for surgery. But with the improvement in surgical technic, only a moderate degree of shock is involved in the operation, and anyone capable of undergoing an ordinary hip-nailing procedure could safely undergo the application of a prosthesis. It is not intended by this statement to minimize the gravity of the operation. Adequate exposure of the hip is required, and the technic of applying the prosthesis must be mastered in detail. The surgeon who attempts this operation without previous training invites disaster, but with such training and experience, it may reasonably be stated that a prosthesis can be applied with no greater difficulty than in most open reductions and hip nailings. X-ray control is not needed. In ordinary cases the operation can be completed in less than sixty minutes and without excess hemorrhage or manipulative shock.

Another point in the selection of cases is to differentiate clearly those in which straightforward hip nailing might reasonably succeed from those in which it is reasonably likely to fail. We believe that this differentiation can be made in the high-neck fractures at the actual subcapital level or very close to it and in both "beak" and comminuted fractures in which no satisfactory reduction can be obtained. But, in selecting these cases as suitable for prosthesis, we also take into consideration the age factor. A patient in the sixties or early seventies, if still active and healthy, deserves every chance for regaining a normal hip. Furthermore, such a patient is less likely than the older patients to suffer from prolonged bed rest. Consequently, even in the face of an added risk of failure, the younger and healthier patients with subcapital fractures are advised to undergo hip nailing followed by longer bed rest, and it is explained to them that if this should fail a secondary prosthetic operation can be done. Only to the older, feebler

patients, who are unlikely to tolerate bed rest or to lead strenuous lives, is the primary prosthesis recommended. It is believed that they will not live to experience any late complications if they do occur.

Technical Considerations

The use of a primary prosthesis can only be recommended because of the technical improvements introduced in the last five years.[2,3] These include the appliance itself as well as the method of inserting it. The present article does not afford space for an extended technical discussion, but the underlying principles deserve mention. The most important point to be learned about the appliance is that a "stem" prosthesis holds so many advantages over the simpler Judet[4] that the latter has fallen into disuse. Although we consider it unwise to say that we would never have an occasion to use it, we are convinced that it should never be used when the bone is osteoporotic or when there is any likelihood that the cortical bone of the neck will fragment or break down under the strain of weight bearing. As a general rule, it is safer to rely entirely on the stem prosthesis, which supplies an artificial neck as well as an artificial head. This not only obviates the danger of necrosis or collapse of the head but also interposes a nonosseous space between acetabulum and trochanter that may lessen the hazard of bridging calcific deposits later on. Choice of the stem prosthesis for the cases in this series has varied between Eicher's instrument and that of Austin Moore, with a strong preference for the latter. Whatever the appliance, it is obviously important for the surgeon to familiarize himself with all the "tricks" required for inserting it. No discussion of the subject would do it justice without a very urgent warning against the dangers that can follow inexperienced handling of the prosthesis, but it should also be observed that no serious difficulty exists for the operator who is well versed in its use.

Selection of the most favorable surgical approach is of paramount importance in the success of this operation. Four standard approaches have been tried in this series of cases: the usual Smith-Petersen technic, its lateral modification, the posterolateral approach of Gibson[5] and the posterior approach advocated by Austin Moore. The two former carry the disadvantage of weakening the anterior structures so that the prosthesis may dislocate in the first postoperative week. This can be prevented by ten days of immobilization with a plaster boot in abduction and internal rotation, but restraint of this sort offers a distinct handicap to convalescence. Gibson's[6] posterolateral approach spares the anterior structures but weakens the abductors and is not considered to offer the same direct ease of approach as that used by Austin Moore, which has gained our unqualified endorsement and can be recommended without reservation in fresh fractures. Its only drawbacks are inability to give free access to anterior structures and the lack of free exposure for reaming out the acetabulum. Both these maneuvers are important in many reconstructive arthroplasties but not in the primary insertion of a prosthesis. In such cases, when Moore's technic is followed, it has often been possible to cut the total operating time to forty minutes. More important than this, the approach imposes minimal shock to the tissues and involves no increased risk of hemorrhage. Direct supervision of the sciatic nerve offers a safeguard against inadvertent stretching and need not be considered an added hazard. Roentgenograms in a typical case are shown in Figure 1. The technic as a whole is so fully described by Moore[3] that further discussion here seems unnecessary.

Postoperative Course

The postoperative care offers few problems. If the anterior approach has been used it is essential to guard against dislocation by maintaining internal rotation and abduction — preferably by a plaster boot with a splint board incorporated in such a way as to maintain internal rotation. However, the posterior approach makes even this precaution unnecessary. It may be wise to allow a few days in bed until the wound heals. However, the patient may be allowed to sit up on the following day if this is considered desirable. The same statement holds for ambulation, which should be begun in the walker or on crutches. From the start the patient may be allowed to rest the foot on the affected side on the floor. This is a great aid to aged people, who ordinarily find the use of crutches difficult to learn. It is often amazing how well these patients are doing as early as the second or third week. Active walking from an early date has proved the most effective means of rehabilitation. Recovery may sometimes come slowly, but encouragement and persistence bring better and better results over the months. Frequently, a case that has reached only fair recovery in the first six months advances to a good result in the second six months. Pain is usually completely absent in the postoperative and convalescent course of most patients.

Complications

In this series of 51 cases there were complications, which can be anticipated when surgery is performed on any group whose average age is in the eighth decade. There were also complications specific for this type of procedure. There were 3 deaths, 1 occurring on the operating table after the conclusion of the procedure, 1 on the thirty-third, and the other on the forty-second postoperative day. These patients were seventy-four, eighty-eight and ninety years of age. The death on the operating table was considered to be due to a pulmonary embolus consequent to manipulation of the entire leg in the course of the operation. The other deaths were from cardiac causes — 1 from cardiac failure, and the other from an acute cardiac infarct. There were 2 additional cases of

pulmonary embolus, both nonfatal and both successfully treated by venous ligations. There were only 3 wound infections, all superficial, with no ensuing disability.

The most striking specific complication — and one that was anticipated when the procedure was first introduced — was the absorption of the neck beneath two of the Judet prostheses. The patients had pain on walking and instability of the hip six months and a year after surgery. X-ray study revealed that the prosthesis had gone into varus, with visible lines of density suggestive of motion between the shafts of the bone and prostheses. One of these prostheses was subsequently removed in another hospital. The other patient has resigned herself to the permanent use of crutches. In retrospect, it is surprising that the complication has not occurred more often. In the reshaping of the neck of the femur for a Moore prosthesis the bone crumbles easily in many cases, and to all outward appearances is totally incapable of bearing weight. Such a situation does not occur when a stem prosthesis is employed, and this is the principal reason for its almost exclusive use. In 2 patients the prostheses became loose and were found to be in considerable varus six months after the operation. This was believed to be due to faulty insertion, the prosthesis being placed in too much varus with poor mechanical weight bearing about the hip. The prostheses were removed and replaced by a Moore reconstruction.

There were 2 dislocations in the series, 1 in a ninety-year-old patient who climbed over the guard rail on the bed on the twenty-eighth day. In both patients the anterior approach had been used; in both, the dislocations were reduced, and the patients suffered no ill effects.

The relatively few complications in this series, in which the prostheses were applied only in fresh fractures of the hip, in comparison with the larger number of complications previously reported,[6] can be attributed to the increased experience we have gained with this method, and in part to a better selection of cases.

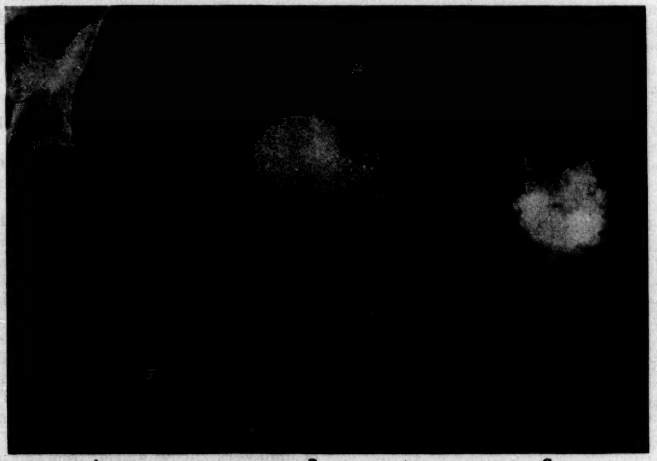

FIGURE 1. *Roentgenograms in an Eighty-Eight-Year-Old Woman, Showing Fresh Fracture (A), Moore Prosthesis As Primary Treatment* (B) *and Appearance of Head of Femur after Removal* (C), *Indicating a True Subcapital Level.*

RESULTS

In considering the results in these cases one must make allowance for confusion arising from associated senile disabilities. For example, ordinary standards do not provide an index for cases in which hemiplegia and fracture are combined. We have based our classification on the patient's recovery as compared with what might be normal for the same person if the hip had not been fractured. *Excellent* indicates a full recovery by this standard. *Good* means moderate impairment of hip function, not significantly limiting the patient's activity. *Fair* implies a definite limitation resulting from the hip fracture, but not enough to cause serious pain or to keep the patient from engaging in reasonably restricted activity. Anything less than fair is graded a failure. In making our evaluations, we have tried to remain as objective as possible, though much is necessarily left to judgment.

The ages of our patients ranged from fifty-five to ninety, with an average of seventy-three. The length of follow-up period varied from two to thirty-five months. Admittedly, this is too brief for final conclusions, but in patients of this age group, short-term successes may represent important benefits. The fact that this preliminary study indicates 13 excellent, 24 good, and 7 fair results out of 51 cases offers significant encouragement for further trial. This leaves 3 unevaluated because of shortness of follow-up period and only 4 failures.

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TREPONEMA PALLIDUM IMMOBILIZATION TEST IN THE EVALUATION OF PATIENTS WITH POSITIVE SEROLOGIC TESTS FOR SYPHILIS*

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ONE of the most perplexing problems that the physician may be called upon to decide is that of the patient with a positive serologic test for syphilis and no other evidence of the disease. Too often the decision is made to give treatment, with the idea that today this is relatively innocuous and easy to administer. Such a course has resulted in the unnecessary treatment of many persons with biologic false-positive reactions. Such therapy has labeled these people as syphilitic, frequently with considerable psychologic, sociologic and economic trauma. Another group of physicians have responded to the problem by assuming that most of these patients were false-positive reactors. The tragedy of this course is seen in those who, because of lack of treatment, subsequently had late manifestations such as neurosyphilis and cardiovascular syphilis.

For many years extensive investigation aimed at producing a more specific test for syphilis has been conducted with the hope of thereby eliminating false-positive reactions. These tests have all depended on the presence of a nonspecific substance known as reagin in syphilitic serum. However, reagin is also found in the serum of numerous nonsyphilitic persons, so that none of these more refined tests have been dependable in eliminating false-positive reactions. In 1949 Nelson and Mayer[1] described a test that was completely different from those previously in use in that it was dependent on the presence in syphilitic serum of an antibody specific for *Treponema pallidum*, an antibody separate and distinct from reagin. This test, known as the *T. pallidum* immobilization test, is based on the immobilization or death of virulent, motile spirochetes on exposure to the specific antibody present in syphilitic serum.

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Method

The test as presently performed in the United States Navy was recently described by Ledbetter and Martens.[2] In brief, it consists of mixing a tissue-free treponema suspension obtained from rabbit testes previously innoculated intratesticularly with virulent *T. pallidum* (Nichols strain), complement (present in guinea-pig serum and necessary for antigen-antibody reaction) and the serum to be tested. After incubation for eighteen hours under anaerobic (95 per cent nitrogen, 5 per cent carbon dioxide) conditions, the percentage of motile organisms is determined by examination with the dark-field microscope. If less than 12 per cent of the spirochetes remain motile the test is interpreted as positive; if more than 70 per cent are motile it is reported as negative. When the percentage of motile organisms is between 12 and 70 the serum is retested, and additional samples obtained if necessary.

As a result of numerous studies by various investigators, the significant features of the immobilizing antibody can be summarized. In the first place it is not found in the serum of normal persons or in that of people suffering from nontreponemal diseases.[3] Secondly, it occurs in the serum of syphilitic persons and in that of patients with three other treponemal diseases — yaws, pinta and bejel.[4] Thirdly, it appears early in the course of syphilitic infection, usually paralleling or lagging slightly behind the building up of reagin; in untreated cases the immobilizing antibody remains throughout life even though reagin may have spontaneously disappeared.[4] Finally, in cases of early syphilis that are treated, the treponema-immobilizing antibody may not reach a sufficient level to cause a positive reaction or, if the test is already positive, may gradually disappear from the blood (but at a rate slower than that of reagin), the test eventually becoming negative. In cases of syphilis of several years' duration, however, treatment usually has no effect on the level of antibody.[3]

This report is based on 17 patients who were referred to the dermatology clinic or ward between January, 1953, and April, 1954, because of positive results on one or more of the reagin serologic tests for syphilis. In no case was there evidence of possible syphilitic infection besides the positive reagin test. To help proper evaluation, treponema-immobilization tests were done on different blood samples as follows: 4 patients had one, 9 had two, and 4 had three. They were performed in the laboratory of the Naval Medical School, National Naval Medical Center, Bethesda, Maryland, representing only a small portion of the total done there during the period of this study. Although the series being reported is small, it is believed that presentation of the salient features of these personally studied cases should lead to a clearer understanding of the use and value of the test.

Results

Treated Patients

Three of the patients had previously been regarded as having early latent syphilis at the time of treatment in 1951, 1944 and 1933 respectively. In each case the reagin tests were weakly positive and spinal-fluid and cardiovascular examinations were negative when the patients were seen in 1953-54. The clinical impression of treated early latent syphilis was confirmed by positive treponema-immobilization tests for each. A typical case report follows:

Case 1. W.Y., after sexual exposure, had a dark-field-negative penile lesion in December, 1932. In April, 1933, and again 1 month later the blood Kahn reaction was found to be ++++. Over the following 7 years he was given several courses of bismuth and arsenic. In December, 1953, a battery of serologic tests showed the blood Kahn reaction to be 2 units, cardiolipin slide positive and Kolmer and Mazzini reactions negative. Treponema-immobilizing tests in January, 1954, were positive. Further therapy was not deemed necessary.

Untreated Patients

Fourteen patients who denied previous treatment for syphilis were seen because of positive reagin tests. In 2 cases the diagnosis of early latent syphilis was made, and this was confirmed by positive treponema-immobilization tests. The following case is illustrative:

Case 4. O.W. was found to have a + Kahn reaction in July, 1952. His last negative reagin test had been 1 year before. Treponema-immobilization tests in October and November were positive. For unknown reasons treatment was not given at that time. On admission to the hospital in January, 1953, the blood Kahn test was 64 units, the Kolmer reaction was 160 units, and Mazzini and Venereal Disease Research Laboratory tests were positive. Spinal-fluid and cardiovascular examinations were negative. A treponema-immobilization test in February was positive. A course of penicillin was then given.

Two patients were suspected of having late latent syphilis. In 1 the diagnosis was fairly certain and was confirmed by positive immobilization tests. The other, however, because of weak reactions on the reagin tests, was considered as a possible false-positive reactor.

Case 7. B.S., a 72-year-old man, stated that in 1908 he had had a penile lesion that was diagnosed as chancroid and treated with a powder. In November, 1950, June, 1951, and December, 1952, when he was hospitalized for other reasons, the blood Kahn reaction was negative. However, in December, 1952, the Kolmer test was positive, and in January, 1953, the blood Kahn reaction was doubtful, the Kolmer test was 8 units, and Mazzini and cardiolipin slide tests were positive. Spinal-fluid and cardiovascular examinations were negative. Two treponema-immobilization tests were positive. The diagnosis of late latent syphilis was made, but treatment was not considered necessary.

Two patients who were believed to be probable false-positive reactors were finally regarded as having latent syphilis on the basis of positive immobilization tests:

Case 8. W.J., a 21-year-old man, was found to have negative Kahn, Kolmer and Mazzini reactions but a weakly positive Venereal Disease Research Laboratory test on January 13, 1954, at the time of premarital examination. A battery of serologic tests 2 weeks later showed the Kahn, Kolmer and Mazzini reactions to be negative and the cardiolipin slide weakly positive. He strongly denied ever having had penile lesions, rash or prior treatment for syphilis, but he recalled having had injections of penicillin for other conditions. Physical examination was negative, as were spinal-fluid and cardiovascular studies. However, treponema-immobilization tests were positive. Further investigation revealed that in 1952, at the time of entry into military service, the blood Kahn reaction had been ++. He did not recall ever having had a blood test before that. All subsequent tests were negative. It was concluded that this man had had syphilis. Further treatment was not deemed necessary.

Case 9. H.B., a 29-year-old woman, on February 17, 1954, during her 7th month of pregnancy, gave the following reactions on a battery of serologic tests: Kahn test, 2 units; Kolmer test, negative; and Mazzini and cardiolipin tests, positive. She denied previous genital lesions, rash or prior treatment for syphilis. Her last negative reagin test had been in September, 1951. Physical examination was negative. The battery was repeated on February 24, with the same results. When the patient was seen 1 week later blood was drawn for a treponema-immobilization test. Because she was leaving to go to another city, where she might not receive proper follow-up study, and in view of her pregnancy it was decided to give treatment despite the clinical impression that she was a false-positive reactor. The immobilization test, however, was reported as positive.

The remaining 8 patients were concluded to be false-positive reactors:

Case 10. F.W., 3 months after an injection of typhoid vaccine, was found to have a ++ blood Kahn reaction, with the same result when the test was repeated. He denied penile lesions, rash and prior treatment for syphilis. Physical examination was negative. One week later the treponema-immobilization test was negative. The blood Kahn test was repeated and also found to be negative.

Case 11. G.A. gave a ++ blood Kahn reaction on December 18, 1953, the day after being vaccinated against smallpox. He denied penile lesions, rash and prior treatment for syphilis. On December 29 a treponema-immobilization test was negative. On the next day the Kahn, Mazzini and cardiolipin slide tests were negative, the Kolmer reaction being 32 units. A second immobilization test on January 13, 1954, was negative, as was the blood Kahn reaction 2 weeks later.

Case 12. W.B., on September 7, 1953, gave a +++ reaction on the blood Kahn and Venereal Disease Research Laboratory tests. Penile lesions, rash and prior treatment for syphilis were denied. In 1949 a blood test had been positive, but no treatment had been given. On admission to the hospital on October 2, 1953, physical examination was negative, and the blood Kahn and Kolmer tests were nega-

tive, and the Mazzini and cardiolipin slide tests positive. Treponema-immobilization tests on October 7 and 13 were negative. Blood Kahn and immobilization tests in March 1954, were negative.

CASE 13. E.B. was admitted to the hospital on July 11, 1953, for acute infectious hepatitis. On admission the blood Kahn reaction was 2 units, the Kolmer test was negative, and Mazzini and cardiolipin slide tests were positive. He denied penile lesions, rash and prior treatment for syphilis, and examination was negative except for the changes associated with the hepatitis. The battery of serologic tests was repeated on July 18, with the following results: Kahn and Kolmer reactions, negative; Mazzini test, positive; and cardiolipin slide test, weakly positive. A treponema-immobilization test on August 28 was negative.

CASE 14. J.D. was told in February, 1953, that his reagin test was positive. The test was repeated 2 weeks later and was negative. On December 17 the blood Kahn reaction was doubtful, the Kolmer test 32 units, and the Mazzini and cardiolipin slide tests positive. A treponema-immobilization test on the same day was negative, as it was when repeated 7 weeks later. A battery of serologic tests on February 19, 1954, gave the same results as that in December except that the blood Kahn reaction was negative and the Kolmer test 16 units; an immobilization test on the same day was negative. On March 19 the Kahn, Kolmer and Venereal Disease Research Laboratory tests were negative, and the Mazzini reaction was doubtful.

CASE 15. N.L. was found to have a doubtful blood Kahn test and a Kolmer reaction of 16 units on December 3, 1953. He denied ever having had penile lesions, rash or prior treatment for syphilis, and physical examination on December 28 was negative. His last negative reagin test had been in October. A treponema-immobilization test on December 28 was negative. Attempts to have him return for follow-up studies were unsuccessful.

CASE 16. C.M. was admitted to the hospital on January 11, 1954, because of acute pharyngitis; the blood Kahn reaction 6 days later was negative. A premarital Kahn test on March 16 was ++++. Penile lesions, rash and prior treatment for syphilis were denied. A battery of serologic tests on March 17 gave the following results: Kahn reaction, doubtful; Venereal Disease Research Laboratory test, weakly positive; Kolmer and Mazzini tests, negative. A treponema-immobilization test on the same day was negative. One week later the battery gave the same results except that the Venereal Disease Research Laboratory test was negative. A treponema-immobilization test on this day was also negative. The Kahn reaction on March 30 was negative.

CASE 17. M.G., a 24-year-old woman, had a doubtful Kahn reaction, Kolmer test of 16 units and positive Mazzini and Venereal Disease Research Laboratory tests on March 16, 1953, during the 1st trimester of pregnancy. Genital lesions, rash and prior treatment for syphilis were denied. Physical examination gave no evidence of syphilitic infection. Treponema-immobilization tests on March 25 and April 14 were negative. The Kahn reaction was negative on April 4 and September 9. She gave birth to a normal baby on September 10. In March, 1954, a battery of serologic tests gave the same results as in March of the preceding year, and a treponema-immobilization test was negative.

DISCUSSION

The specificity of the treponema-immobilization test is now generally accepted. Biologic false-positive reactions occur only in cases of yaws, pinta and bejel — diseases due to treponema that are closely related to that of syphilis. False-positive reactions because of laboratory errors are seen in a small percentage of cases, but most of these are readily detected by the use of proper controls.

It is known that the immobilizing antibody develops during early syphilis, gradually increasing in amount. As a result, false-negative reactions may be obtained when the test is performed before the level of antibody has reached a level sufficient to give a positive reaction. Nelson et al.[4] found that 62 per cent of patients with dark-field-positive primary syphilis had positive immobilization tests, whereas these tests in 100 per cent of cases of dark-field-positive secondary syphilis were positive. Thompson and Magnuson[5] reported that only 90.8 per cent of their patients with secondary syphilis had positive treponema-immobilization tests. In early syphilis, however, other adequate means of diagnosis, particularly the dark-field examination, are available.

The fact that a negative immobilization test does not rule out the possibility of early syphilis must be kept in mind. Case 14 might be cited as an example. It is possible that this patient was in the primary stage with a concealed chancre. Although he was considered a probable false-positive reactor, inadequate follow-up study prevented a definite conclusion to that effect. In such cases repeated reagin and treponema-immobilization tests are desirable.

It is in cases requiring differentiation of latent syphilis and biologic false-positive reactions that the immobilization test is most useful. It is positive in all cases of untreated latent syphilis. Treatment may result in reversal to negativity in some cases of early latent syphilis. Of the 17 patients with positive reagin tests covered by this report, a positive treponema-immobilization test was obtained in 9. Three patients with previous diagnoses of and treatment for early latent syphilis gave positive reactions, confirming the earlier diagnosis. The diagnosis of latent syphilis was made in the other 6, the immobilization test being particularly valuable in 3 cases. Follow-up studies in 7 of those with negative immobilization tests confirmed the fact that they were biologic false-positive reactors; Case 14, as previously pointed out, was probably in the same classification, but adequate follow-up examination was not possible.

The treponema-immobilization test, it should be mentioned, is positive in all cases of untreated cardiovascular syphilis, neurosyphilis, gummas and congenital syphilis. In patients with late manifestations it is positive even though the reagin tests have become negative.

In evaluating the patient with a positive treponema-immobilization test one must remember that this in itself is not an indication for treatment. A positive test merely indicates that the person has or has had a syphilitic infection. Whether or not therapy should be given must be decided on the basis of the trend of quantitative reagin tests and on the adequacy of any previous treatment given.

The treponema-immobilization test, as presently performed, is a complicated procedure requiring expensive supplies and trained personnel. To my knowledge, there are only 11 laboratories in the United States that are now performing the test or

plan to do so in the near future. They are as follows: Venereal Disease Experimental Laboratory, Chapel Hill, North Carolina; Division of Venereal Disease, United States Public Health Service, Chamblee, Georgia; Johns Hopkins School of Hygiene and Public Health, Baltimore, Maryland; Department of Dermatology and Syphilology, University Hospital of Michigan, Ann Arbor, Michigan; Department of Dermatology and Syphilology, Columbia University College of Physicians and Surgeons, New York City; Dr. Charles Rein, 580 Fifth Avenue, New York City; Division of Laboratories and Research, New York State Department of Health, Albany, New York; Department of Serology, Army Medical Center, Washington, D.C.; Treponema Pallidum Immobilization Laboratory, United States Naval Medical School, National Naval Medical Center, Bethesda, Maryland; Los Angeles County Department of Health, Los Angeles, California; and Dade County Health Department, Dade County, Florida.

Summary and Conclusions

Seventeen patients with positive reagin serologic tests for syphilis are evaluated on the basis of results of the treponema-immobilization test.

The test is a valuable diagnostic tool, particularly in the differentiation of latent syphilis and biologic false-positive reactions.

The establishment of additional laboratories for the performance of the test, to make it more generally available to the practicing physician, is desirable.

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TETRACYCLINE IN GENITOURINARY INFECTIONS*

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BOSTON

THE most recent major addition to the antibiotic armamentarium of the practicing physician has been the broad-spectrum antibiotic tetracycline.‖ This compound is closely related to both chlortetracycline†† and oxytetracycline‡‡ in chemical structure, pharmacologic properties and antimicrobial activity in vitro.[1,2] Early clinical trials suggest that gastrointestinal irritation is less frequent with tetracycline than with either of the other analogues, chlortetracycline or αxytetracycline.[2]

The present study is a comparison of the in vitro sensitivity of 200 strains of bacteria, recently isolated from patients with infections of the genitourinary tract, to tetracycline and the more commonly used antibiotics: penicillin, streptomycin, chloramphenicol,** chlortetracycline and oxytetracycline. These strains were the causative organisms in clinical infections. On some of these patients controlled therapeutic trials were carried out to correlate in vitro sensitivity levels with clinical response.

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Methods and Materials

The bacterial strains accepted for this study were isolated from patients with infections of the genitourinary tract between November, 1953, and March, 1954. In all cases the strains were considered to be the causative infecting agents. The basis for bacterial diagnosis was the presence of significant numbers of organisms seen in stained smears of the urinary sediment and more than 1000 bacteria per cubic centimeter of urine as determined by quantitative colony counts using tryptic digest agar poured plates into which 0.001 to 1.0 cc. of fresh urine was incorporated. Identification of all bacterial strains was based on standard cultural characteristics and biochemical fermentation reactions. Most of these infections either were refractory to previous treatment or had run a chronic course. A few infections were acute or primary. For these reasons the majority of patients had received at least one antibiotic in the past; however, none had received tetracycline.

Sensitivity studies were carried out with a modification of the two-fold tube-dilution technic of Braude and Dockrill.[3] Concentrations of freshly prepared anti-

biotics ranging from 2 to 32 microgm. per cubic centimeter were employed. Inoculums, consisting of approximately 10^6 organisms in the logarithmic phase of growth, were placed in tryptose phosphate broth (Difco) containing the antibiotic. After eighteen hours of incubation at 37°C. the test was read to determine: the tube showing relative bacteriostasis — that is, the one that showed the greatest decrease in growth, though slight growth might be present; and absolute bacteriostasis — that is, no increase in the amount of growth over the initial inoculum. Clinical responses correlate most closely with the results read as relative bacteriostasis; hence, only these results are included in this report.

The patients studied were both adults and children with significant infections, all of which had been present at least one week before therapy was begun. The underlying mechanisms involved in the pathogeneses of the diseases were varied, as were the bacteria isolated and the in vitro sensitivities of these bacteria. Most of the group received 1.0 gm. of tetracycline daily in divided doses over a ten-day period. Cultures were done before initiation of and after termination of therapy and frequently during therapy. In all cases quantitative bacterial counts were done, thus minimizing confusion over unrecognized contamination at the time specimens of urine were collected.

TABLE 1. *Sensitivity of Strains to Various Antibiotics.**

BACTERIAL STRAIN	NO. OF STRAINS	STRAINS SENSITIVE TO TETRACYCLINE	STRAINS SENSITIVE TO STREPTOMYCIN	STRAINS SENSITIVE TO CHLORAMPHENICOL	STRAINS SENSITIVE TO CHLORTETRACYCLINE	STRAINS SENSITIVE TO OXYTETRACYCLINE	STRAINS SENSITIVE TO PENICILLIN
A. aerogenes	48	22	6	30	21	20	—
Proteus	31	6	5	11	8	5	—
Esch. coli	31	18	7	28	24	21	—
Pseudomonas	17	10	2	3	9	10	—
Miscellaneous gram-negative organisms	31	21	10	24	25	20	—
M. pyogenes var. *albus*	15	9	—	6	8	5	4
M. pyogenes var. *aureus*	7	1	—	2	1	0	0
Enterococci	20	6	—	9	7	5	17
Totals	200	93(46.5%)	30†(19%)	113(56.5%)	103(51.5%)	86(43%)	21‡(50%)

*To level of 32 microgm./cc. or less.
†Total number, 158.
‡Total number, 42.

RESULTS AND DISCUSSION

The strains of bacteria isolated and the number of each strain sensitive to a level of 32 microgm. per cubic centimeter or less of the various antibiotics are presented in Table 1. Gram-negative strains of bacteria constituted 79 per cent, and gram-positive bacteria the remaining proportion of the 200 strains studied. Resistance or sensitivity to a given antibiotic is more constant and predictable on a species than on a tinctorial basis. *Escherichia coli* and the miscellaneous gram-negative bacteria as a group are quite sensitive to the tetracycline analogues and to chloramphenicol. The majority of strains of *Aerobacter aerogenes* and proteus species are resistant to the tetracyclines. In the bacterial strains studied, with the exception of pseudomonas (pyocyaneus), a close correlation exists between in vitro sensitivity and clinical response to treatment. For pseudomonas there is often a discrepancy between in vitro findings and clinical results,[4] at least with oxytetracycline. The

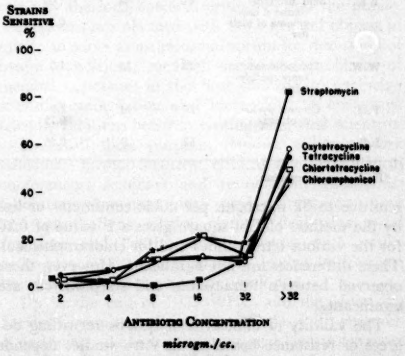

FIGURE 1. *Sensitivity of Bacterial Strains to Antibiotics.*

gram-positive cocci, consisting of *Micrococcus pyogenes* (*staphylococci*) and enterococci, are quite resistant to tetracycline, penicillin, chlortetracycline and oxytetracycline; only 38.1 per cent are sensitive to tetracycline. This suggests that the development of resistance to either chlortetracycline or oxytetracycline may result in the acquisition of crossresistance to tetracycline as well as to the other member of the

group. With representative bacterial strains cross-resistance among the three analogues has been induced in vitro.[2] However, it must be emphasized that specific conclusions regarding any strain are not justified without testing in vitro.

Comparison of the proportion of strains sensitive to a given level of tetracycline with the proportion sensitive to chlortetracycline, chloramphenicol and oxytetracycline reveals only minor differences (Fig. 1). Statistical comparison of the number of strains sensitive to 32 microgm. per cubic centimeter or less by the method of Chi square gives a P value of 0.20 for the various tetracyclines and for chloramphenicol. These differences are not significant. However, those observed between tetracycline and streptomycin are significant.

The validity of clinical assumptions regarding degrees of resistance based on in vitro studies depends on the correlation between the sensitivity test and clinical results. Table 2 presents data observed in 13 patients with infections due to bacteria of different known in vitro sensitivities. These patients were treated with tetracycline. Therapy was successful in those harboring bacteria sensitive to 32 microgm. per cubic centimeter or less of tetracycline in vitro. At the level of 32 microgm. the improvement was classified as good in most cases; specifically, a good response was one in which the causative bacteria were eliminated, although reinfection or superinfection with other strains subsequently occurred. Of the 2 persons with mixed infections, the patient with two sensitive strains responded well (A.T.); the other (L.K.), in whom there was a sensitive pseudomonas and resistant *A. aerogenes* and *M. pyogenes* var. *albus*, failed to respond. The latter problem is common in this type of infection, particularly when contributing mechanical factors are irremediable. Similar observations carried out with the other antibiotics included in this comparison showed that bacteria sensitive to 32 microgm. per cubic centimeter of chloramphenicol also will respond favorably; those sensitive to 16 microgm. of chlortetracycline and of oxytetracycline will respond quite uniformly, whereas at a bacterial sensitivity level of 32 microgm. per cubic centimeter the clinical response is variable. In this respect tetracycline compares quite closely with the other two analogues, though favorable results are more uniform at the sensitivity level of 32 microgm. This conforms with the observations of Finland et al.[2] that after an oral dose of tetracycline the serum levels are slightly higher than after the same dose of chlortetracycline and of oxytetracycline.

In this small number of patients untoward side effects were noted in 2: in 1 there was frank diarrhea lasting fourteen days after discontinuance of the drug; in the other there was an asymptomatic increase in

TABLE 2. *Resistance of Various Infecting Organisms to Tetracycline.*

PATIENT	DIAGNOSIS	AGE	SEX	DOSAGE	DURATION OF THERAPY	ORGANISM	IN VITRO SENSITIVITY	THERAPEUTIC RESULTS
		yr.		gm./day	days		microgm./cc.	
E.H.	Nephrolithiasis	65	M	1.0	7	*Esch. intermedium*	2	Excellent
M.B.	Chronic cystitis	30	F	1.0	4	*M. pyogenes* (var. *albus*)	2	Excellent
A.T.	Benign prostatic hypertrophy	69	M	1.0	4	*Esch. freundii*	2	Good
A.T.	Phimosis & cystitis	11	M	0.75	7	*Esch. coli*; *M. pyogenes* (var. *albus*)*	4	Excellent
J.C.	Acute urethritis	26	M	1.0	14	*M. pyogenes* (var. *albus*)	4	Excellent
S.H.	Acute cystitis	9	F	1.0	6	*Esch. coli*	4	Good
E.S.	Chronic pyelonephritis	61	F	1.0	9	*Klebsiella pneumoniae*	16	Excellent
M.H.	Chronic cystitis	26	F	1.0	8	*Streptococcus faecalis*	32	Good
M.I.	Acute urethritis	20	M	0.75	8	*M. pyogenes* (var. *albus*)	32	Good
L.K.	Skin ureterostomies & carcinoma of bladder	69	M	1.0	5	*Pseudomonas aeruginosa*;	16	
				0.5	9	*A. aerogenes**; *M. pyogenes* (var. *albus*).	128	None
W.W.	Postprostatectomy epididymitis	73	M	1.0	9	*A. aerogenes*	128	None
P.H.	Chronic pyelonephritis	27	M	1.0 0.75	4 8	*Paracolobactrum intermedium*	>256	Good (subjective)
L.B.		52	F	0.75	13	*Proteus vulgaris*	>256	None

*Predominant organism.

In this small number of patients untoward side effects were noted in 2: in 1 there was frank diarrhea lasting fourteen days after discontinuance of the drug; in the other there was an asymptomatic increase in

the number of stools from one every other day to three to five a day.

Conclusions

Tetracycline is a useful drug in the management of genitourinary infections. Correlation of in vitro sensitivity tests with clinical results suggests that approximately 45 per cent of strains isolated from the urinary tract can be expected to respond to treatment if complicating mechanical factors are also alleviated. For any species of bacteria this percentage may be higher or lower, and no specific conclusions regarding a given strain are justified without in vitro testing. Tetracycline cannot be used routinely as an alternative agent for infections resistant to chlortetracycline or oxytetracycline, since crossresistance to these analogues is common though not absolute. When sensitivity tests indicate that each of the tetracycline family of antibiotics is equally effective, tetracycline itself may be preferable because of the low prevalence of side effects, its stability, its solubility and the possibility of slightly greater absorption from the gastrointestinal tract.

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SPECIAL ARTICLE

SOME IMPRESSIONS OF TEACHING MEDICAL MISSIONS OF THE WORLD HEALTH ORGANIZATION*

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NEW YORK CITY

On April 7, the World Health Organization (WHO) of the United Nations (UN) celebrated its sixth anniversary, and, in commemoration of the occasion, World Health Day was proclaimed by the President of the United States. The important contribution that this international agency is making to world health impels me to recount some first-hand experiences I have had with one segment of the educational and training programs: the "teaching medical missions," now known as "visiting teams of medical scientists." The name was changed in 1952 to eliminate the patronizing adjective "teaching" and any sectarian implications attached to the term "mission."

WHO is now in its seventh year of existence. Its scope of activities includes public health and environmental sanitation, maternal and child health, nutrition, mental health, epidemic diseases, standardization of drugs and health statistics; it provides technical and advisory services as well as operating programs in these and other areas; its annual budget for 1954 is around $9,000,000, contributed by 75 active and associate member countries.

Visiting teams of medical scientists are voluntary projects always initiated by invitation from an official agency of a member nation, usually the Ministry of Health. The host country invites WHO to send representatives in selected specialties to be the guests of the government. If the project is approved, WHO picks a traveling faculty of 8 to 14 international members and, in collaboration with a local preparatory committee, arranges the programming and time schedule of a visit of two weeks' to two months' duration. The visiting group is assured a cordial welcome by the local medical profession and the public.

Programs are planned with three general objects in mind: to serve as an informal forum for discussion of health conditions, medical needs and problems of medical education in the host country; to exchange scientific information and ideas; and to encourage friendly relations between visiting and local scientists.

To fulfill these purposes requires a heavy work schedule: formal lectures; clinical and pathological conferences; seminars and round-table discussions; laboratory demonstrations, ward rounds, operations and consultations; motion pictures, field trips, social functions and "curbstone" discussions with native colleagues in various specialties, twelve to fourteen hours comprising the average work day.

Up to the end of 1953 WHO and the Unitarian Service Committee of the United States, both separately and jointly, have sent international faculties to more than 70 universities in 17 foreign countries of South America, Europe and Asia. A total of 175 men have served on these visiting teams. They came from 45 American and from 20 non-American institutions. I have been on 5 such teams and committees: in Poland and Finland in 1948, Switzerland in the spring of 1950, the Netherlands and Sweden in the fall of that year, Israel and Iran in 1951 and India in 1953.

These assignments provide background material bearing on two questions sometimes raised by the

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public, the medical profession and even by persons in government. The first is whether participation by the United States in WHO is contributing substantially to world health, good will and peace or whether this country should withdraw from the international agency and embark on an expanded program of its own in world health promotion. The other is whether these visiting teams of medical scientists provide useful technics of medical education.

I should like to give some reasons, based in part on personal experience, why I believe that in the nonpolitical sphere of health and medicine, international co-operation among groups of nations is more effective than any bilateral arrangements. This view is recognized in the American Point 4 Technical Assistance Program, as re-emphasized by former President Truman, originator of the plan, in a recent television broadcast on March 7 of this year.

Free choice of a visiting faculty from all countries of the world is the best way to ensure professional competence. No nation has a monopoly on medical advances: insulin was discovered by a Canadian, penicillin by a Scotsman, streptomycin by an American, and DDT by a Swiss. Members of the 5 visiting teams to which I was assigned came from 40 universities in 15 countries of 6 continents. Four Nobel prize winners in medicine—Dam, of Denmark, Tiselius, of Sweden, Fleming, of the United Kingdom, and Heymanns, of Belgium—were members of the visiting teams to Sweden and India.

Recognition by the host country of the professional competence of these international faculties was manifested on many occasions. The government of Israel requested the 3 public-health representatives of the team, 1 Norwegian and 2 Americans, to act as official advisers on problems of immigration, sanitation, epidemiology and public-health administration. A number of their recommendations were accepted, and when the mission ended, Dr. Sheba, director general of health, stated, "It was a genuinely important event in Israel medicine." This seemed to be a true statement if one judged from the record attendance of local doctors at the different sessions.

The dean of the medical school in Teheran had all the lectures by members of the visiting team translated into the Persian language and published in book form for country-wide distribution to the doctors of Iran. The original manuscripts were in 4 languages.

The fact that WHO is strictly a technical body, free from all political and religious ties and international in its outlook, has gained for it the confidence and respect of all the free nations of the world, in the East as well as in the West. This trust was demonstrated when a visiting team was permitted, as late as the fall of 1951, to travel from Israel, a Hebrew nation, directly to Iran, a Muslim country. Iran was willing to accept the WHO principle that disease and the fight against it know no national or religious boundaries. This international point of view was affirmed by Shah Reza Pahlevi in his audience for the visiting team at the close of the mission.

Equally gratifying was the response of the students. The applause that followed the first interdepartmental clinical conference ever to be held in Iran presaged the introduction of a new pedagogic technic in the curriculum. In Iran the expressed wish of the student body in 1951 was virtually tantamount to approval by the faculty.

The team even received a warm welcome in Poland in 1948 just before it went under Russian domination. A dramatic incident that occurred soon after its arrival helped a good deal. The majority of the members of the visiting team were American; 2 were British, and 1 each was Swiss, Swedish and Czechoslovakian. One night, while asleep in a hospital constructed by the Unitarian Service Committee in the south of Poland, we were awakened by the emergency admission of a youngster ten years of age who had ruptured his kidney in an automobile accident. To save his life an immediate operation was required, but a transfusion was equally urgent to prevent exsanguination. In the absence of functioning blood banks the American as well as the other doctors on the team volunteered to donate blood. The child survived, and, the next morning, headlines appeared in the Polish newspapers: "American professors bleed for Poland."

Reaction to the six weeks' visit to that country was revealed by letters from such diverse sources as the chairman of the Polish Faculties of Medicine and the United States Embassy in Warsaw. The Polish letter read as follows:

> You came to us bringing gifts without asking anything in exchange. You brought great gifts in both hands. In the right hand you brought us the achievements of science for which we were so hungry. In the left hand you brought us a different gift. This gift is a friendly, human attitude. For both of these gifts we owe you gratitude.

The letter from the United States Embassy was as follows:

> I should like to express my gratification at the achievements of the Medical Mission, both in spreading medical knowledge and in promoting good will among nations. I am naturally happy that so many physicians and surgeons from the United States took part in the Mission. Yet I am no less happy that these physicians worked as part of an international team under the auspices of the W.H.O. and that their individual practices were pooled in a single cooperative undertaking.

It is regrettable that, since 1948, Poland has been taken completely into the Soviet orbit and that it and all the other satellite countries have withdrawn their support of WHO.

Acceptance in the technical field of health of practical, effective international co-operation on all professional levels in the Near East and in Northern Europe is extremely significant when viewed against their turbulent political backgrounds.

Many underdeveloped countries of Asia and Africa have recently gained their freedom, and there is an intense upsurge of national feeling. They will fiercely resist any suspicion of encroachment on this newly

won freedom. One does not need to be a cultural anthropologist to know that in those areas of the world visiting teams of international composition are less likely to offend the sensitivity of their hosts and are less suspect than a purely national group from a foreign country, however well intentioned that country may be.

Resistance to visiting groups of national origin is understandable when viewed against the historical background of many of these countries. In Iran more than 90 per cent of the faculty members of the 5 medical schools received their education in France, whereas in India the United Kingdom continues to dominate medical theory and practice; in Japan the German influence is still strong. A team of doctors from one country—America or any other, without French, British and German representation—would very probably be resented by the native medical counterparts in the respective countries. Chester Bowles,* in commenting on the Western conflict with Communism as a world force, says, "There is a fundamental limitation on American information programs and it raises the question whether the democratic forces in the world do not need an international rallying point which transcends any one nation." If this is true in the sphere of political ideology how much more true is it for the field of health, which by its very nature is, or should be, global in its outlook and scope of operations!

The wide acceptance of visiting teams of WHO in academic and governmental circles of its member nations establishes these projects as a valuable medium of world health promotion as well as a useful educational technic. It reflects the care with which WHO has picked its teams irrespective of origin or country, and the efforts put into preparatory planning, scheduling and day-to-day operations while the team is in residence in the host country.

The personal contact, the informality of discussions and the recognition by all participants, visiting and local, that the interchange of scientific information is in a real sense a two-way street of education remove the stigma of loss of face, encourage free and frank discussion and can lead to friendly and often lasting relations.

At our departure from India in 1953 Dr. Rajagopalachari, the chief minister of Madras State and one of the current sages of India, had this to say:

> We have never seen men and women of your eminence actually working with the local people as if you had been employed by us to work here. This has thrilled our people. Aside from the scientific work, the very human side they saw really thrilled them. They have seen for the first time medical men who have looked upon their science as, so to say, a fine art.

Indians, sensitive Asians, and people the world over instinctively respond to visitors who treat their people as people and not as source material for the amassing of data and statistics.

*Bowles, C. *Ambassador's Report*. 415 pp. New York: Harper, 1954. P. 318.

I did not feel this warm acceptance during my first ward rounds with medical students and house officers shortly after arriving in India. I remember how my chagrin kept growing as I watched the horizontal nods in unison that accompanied my talks. This sign of noncomprehension was especially disconcerting because I already knew that it was not due to language difficulties. Only later did I learn with great relief that a negative shaking of the head is the conventional sign of understanding and approval in India.

Language barriers, incidentally, presented a problem in only a few of the visited countries. Only in Poland and Iran were interpreters needed; in Finland, Sweden, the Netherlands, Switzerland, Israel and India the English language of either the pure British or tainted American variety proved a suitable medium of exchange.

Of no less importance to the traveling group are the benefits that accrue to the visitors themselves. The stimulus of living intimately for two months with foreign colleagues who have similar interests is great. Equally rewarding are the opportunities to talk to people from remote lands, to hear strange tales, to eat bizarre foods, to join in unusual social functions, to see exotic diseases and to learn about foreign cultures. A few memorable experiences were a scholarly address by an Iranian bibliophile on Avicenna and Rhazus, the two great Persian physicians of the first millennium; a swim in the Caspian Sea with Iranian colleagues; sweating it out in a sauna (akin to a Turkish bath) with Finnish colleagues; a picnic on top of the Tatra Mountains along the border of Czechoslovakia and Poland; feasting on chalotkabob in Iran and breaking bread with an Arab sheik in Israel; a moonlit view of the Taj Mahal in Agra; and examination of patients with such textbook diseases as Madura foot, guinea-worm infestation, leprosy, schistosomiasis, leishmaniasis, filariasis, kwashiorkor, cholera and tropical eosinophilia.

But even more pervasive than specific memories, however dramatic they may be, is the over-all conviction that all the peoples of the world, white and black, yellow and brown, are essentially alike. Their basic desires are the same: to be healthy, to be free, to be respected, to have enough food to eat and enough clothes to wear and to have shelter over their heads. Fulfillment of these basic needs brings hope and faith in their wake; without them there is pain and suffering, insecurity and despair.

Another stirring impression that one carries away is the rich reservoir of potential friendship for Americans as people that exists throughout the world, in the East as well as in the West. This potential reservoir could be realized if as many Americans as possible obtained first-hand experience of working with foreign colleagues in other lands. In no better way can mutual understanding and respect be achieved. In Iran, in India and in other countries, Danish doctors were conducting antituberculosis campaigns by mass

BCG inoculations, Italian public-health workers were helping to eradicate malaria with DDT, Swedish nurses were attending children in hospitals, and American immunologists were vaccinating babies against smallpox, all working together for world health promotion.

The medical and paramedical professions speak a universal language, have a common goal and enjoy the confidence of all peoples. To quote Dr. Roger I. Lee: "The humanitarian aspect and the universality of medicine, its language, its aim, and its ideals are certainly at this time a most cogent implementation for World Peace."

The yearly investment by the United States in WHO of about 1 cent per $1000 of national income, or less than the cost of a 3-cent postage stamp per capita, is small indeed when measured against the huge returns of increased productive labor, higher standards of living and world amity.

WHO, in its global fight against disease, is doing its share to bring this about in an unobtrusive but highly practical way. Such constructive programs of technical assistance and training designed to win the trust of the peoples of the free world can effectively supplement the armed might of military machines as guarantees of world peace.

MEDICAL PROGRESS

RESUSCITATION AND OTHER USES OF ARTIFICIAL RESPIRATION (Concluded)*

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BOSTON

Gravity Methods

Cyclic tilting of the long axis of the body has proved to be a valuable aid to respiration, particularly in the convalescent phase of respiratory poliomyelitis.[50,51] Shifting of the abdominal contents causes a piston-like action of the diaphragm that is fairly effective in ventilating the lungs; there is much less evidence for the circulatory acceleration said to accompany the respiratory oscillations.[52]

The rapidly rocking bed has at least two purposes in patients with poliomyelitis. When some respiratory-muscle power has returned the patient can emerge from the tank respirator periodically and for progressively longer intervals, profiting from greater freedom and easier nursing attention. A further possible advantage is prevention of skeletal demineralization and its accompanying renal complications; this action has been found in normal subjects during forced immobilization[53] but is not clearly established in patients with poliomyelitis.

By a modification of the technic of Asmussen and Nielsen[54] the ventilatory effectiveness of the rocking bed has been evaluated[55]; the procedure involves measurement of changes in resting end-expiratory lung volume when the bed is stopped momentarily at different declinations from the horizontal position. Operating through a maximal excursion the bed is capable of ventilating adequately some totally paralyzed patients, but this is not true if lung or thoracic compliance is much reduced.

The rocking method has been recommended for resuscitation of the newborn.[56] Although some assistance to respiration undoubtedly occurs in babies who have breathed, it has not been shown that the force of gravity acting during rocking through an arc of even 90° is capable of initiating the inflation of airless newborn lungs. Manual rocking through an arc of as much as 180° has been practiced for many years as a method of neonatal resuscitation; there is little evidence of its effectiveness.[7]

Pressure-Breathing Devices

Most extensively used devices for prolonged artificial respiration are various forms of apparatus that create a pressure difference between the air passages and the outside of the body. Simple analogous forms are mouth-to-mouth insufflation and manual compression of an anesthesia bag; these methods constitute what is called intermittent positive-pressure breathing if expiration occurs at nearly atmospheric pressure. In principle other forms are similar, whether an anesthesia bag is compressed cyclically in an automatic manner, a face mask is used or the pressure around the body is cyclically lowered below atmospheric pressure, with the lungs remaining at atmospheric pressure.[57]

Body and Cuirass Respirators

The intermittent positive-pressure breathing obtained by enclosure of the patient's body in a tank (Drinker) respirator remains the standard method of treating patients with severe respiratory-muscle insufficiency. This method has also been called, unfortunately, "intermittent negative-pressure breathing." To a patient in a tank respirator inspiration happens when intrapulmonary pressure becomes *positive in*

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relation to the pressure around his body. Except for a minor difference in ventilation caused by gas-density changes in the lungs there is no difference between this type of breathing and that caused by elevation of pressure in a face mask. The inconveniences of the body respirator are more than counterbalanced by its effectiveness and safety. It is of interest that the anesthesia-bag method applied to tracheotomy tubes was used on a large scale in the severe Danish epidemic of poliomyelitis in 1952; medical students and nurses were responsible for round-the-clock squeezing of the anesthesia bags.[58] This experience has stimulated the development of a variety of mechanical substitutes for the student.

Recent studies of the respiratory mechanics of poliomyelitic patients are helpful in the utilization of respirators.[27,59,60] Since the lungs and chest have significant and variable reductions of distensibility in poliomyelitis the criterion of adequate respirator settings should be the pulmonary ventilation of the patient, not the pressure reading of the gauge. Lung distensibility can change quickly because of atelectasis, respiratory obstruction or pulmonary edema, so that pressure settings must be adjusted accordingly to maintain adequate pulmonary ventilation.

Spirometer tracings of lung-volume changes corresponding to tank-pressure changes have provided a means of quantitating the effectiveness of any respiratory device.[60,61] By this technic the comparative actions of tank and cuirass respirators have been measured.[55,62] A cuirass that covers the abdomen and the anterior part of the chest is much more effective than one covering only the anterior portion of the chest, but is much less effective than a tank. Although less effective than a body respirator in terms of pulmonary ventilation, the cuirass respirators (as well as rocking beds) have proved exceedingly valuable in the convalescent phase of poliomyelitis, when respiratory-muscle function is recovering.

Resuscitators

A resuscitator may be defined as a device that creates pressure changes in a face mask or the upper airway, thereby causing ventilation of the lungs (if the air passages are sufficiently unobstructed and the lungs are capable of being inflated). Some resuscitators, manually controlled, consist of a hand bellows or pump, or of a special valve that delivers oxygen from a cylinder; in these devices the shape of the mask pressure curve is in the hands of the operator, who should therefore be highly skilled. Automatically cycling devices are used by relatively untrained lay as well as professionally trained persons. Cycling is controlled by mask pressure changes, by a timing mechanism or by a fixed volume stroke. Numerically, the first type is by far the most common, and most research has been confined to this class.

In the pressure-cycled resuscitators the mask pressure may fluctuate above atmospheric pressure throughout the respiratory cycle, or expiration may include a subatmospheric phase. All resuscitators, particularly the positive-negative type, have been criticized from time to time because of valid or sometimes unsubstantiated claims that the positive phase might overdistend the lungs, that the negative phase might injure lung tissue and cause pulmonary edema, that the airway pressures might adversely affect the circulation and that the devices are unreliable. Recent studies have permitted a sounder appraisal, based primarily on more extensive examination of the circulation and on realization of the interrelations between pressure-flow characteristics of the device and mechanical properties of the patient. The extent of practical usefulness of resuscitators remains a subject of debate.

Effects on Respiration

Devices employing positive mask pressure only rely upon the pressure from a source of compressed gas to inflate the lungs; a tripping mechanism is set to cycle at a desired level of mask pressure, allowing expiration to proceed passively through another path. The flow of gas into the lungs is opposed by the resistance to flow and by the elastic recoil of the lungs that builds up pressure progressively and ultimately causes cycling. If the compliance and resistance of the respiratory system were known one could predict the tidal volume for any level of mask pressure (assuming that expiration proceeded to essentially atmospheric pressure). If resistance were high the initial flow rate would build up pressure immediately, and if the tripping level were reached thereby, the device would cycle rapidly back and forth between expiratory and inspiratory positions. This "chattering" provides immediate warning that serious airway obstruction is present.

In the positive-pressure type expiration occurs as the distended lungs force air out through the expiratory path; because of resistance mask pressure remains above atmospheric, much more so early in expiration, when flow is highest. As mask pressure falls, with decreasing flow, a tripping pressure level is reached, at which inspiration again begins. The positive-negative-pressure resuscitators differ by having an active expiratory phase, usually obtained by a venturi orifice. With such venturi orifices, which are designed for good mechanical reasons, elastic recoil during the first part of expiration tends to force air out at a high rate, the mechanism acting as a resistance, and mask pressure remains positive. Late in expiration the instrument tends to aspirate air while the thorax progressively resists expiration, and mask pressure falls below atmospheric.

The respiratory effects of resuscitators depend on the ventilation pattern induced by the mask-pressure changes and the consequences of this pattern on ventilation distribution and gas exchange. The details of the latter processes are not thoroughly known. The concepts that follow are therefore subject to revision

when more is known about the architectural form of lungs inflated by different types of artificial respiration, the effects of such differences, if any, on alveolar ventilation distribution and the effects, on pulmonary capillary flow, of local variations in alveolar distention as well as changes in rates of flow through the lung circulation as a whole.

In the studies reported, resuscitators have proved capable, with few exceptions, of giving at least adequate alveolar ventilation to patients requiring artificial respiration. To state how well they perform in the hands of firemen and other rescue workers would require knowledge, which is not available, on the distensibility and resistance of the lungs of apneic patients as well as other factors. There is no doubt that in some apneic persons lung distensibility is so low that a resuscitator would cycle very rapidly and ineffectively; similarly a high resistance would cause failure to provide adequate ventilation.

Because a given excursion of airway pressure below atmospheric usually causes less ventilation than an equivalent change above atmospheric the positive-pressure phase is relatively more effective (except when the upper limits of lung inflation are approached). Furthermore, a given inspiratory pressure swing will be more effective if it starts from atmospheric pressure, rather than from subatmospheric pressure, especially in the presence of pulmonary edema.[25] This is because the lungs, when collapsed, require energy to overcome surface tension as well as tissue elasticity. The extent to which the negative phase collapses terminal air passages is not known, but such a result would be consistent with the above observations on compliance and with the evidence for possible impairment of distribution of ventilation. If blood flow continued through collapsed alveoli the level of arterial oxygen tension (pO_2) would be lower than alveolar pO_2 by an amount that is greater for resuscitators having a negative phase. Greene et al.[63] have reported data that support this possibility. The difference in arterial pO_2 when positive-pressure devices are compared with positive-negative devices may be significant when the machines are operating on compressed air. When high oxygen is present in the lungs, however, even fairly gross abnormalities of ventilation distribution are of no practical significance.

All the respiratory effects of the negative phase described above represent disadvantages, though they can be countered by a sufficient increase in inspiratory positive pressure. Another disadvantage often referred to is the discomfort, or "bucking," that occurs when a spontaneously breathing patient attempts to inspire or expire at flow rates greater than those that the machine provides. This objection, usually made when a normal subject tests a resuscitator on himself, can hardly be said to apply to apneic patients, for whom resuscitators are designed. Nevertheless, it is logical to question why a negative phase should be considered, unless it conveys some special advantage. The most important reason is to permit maximal variation of mask pressure with the lowest possible mean mask pressure and without resort to dangerously high inspiratory positive pressure.

Circulatory Effects

Circulatory alterations during artificial respiration have continued to attract a major share of attention.

Maloney and his associates[64] related the mean mask pressure in anesthetized patients to cardiac output and arterial blood pressures, in essential respects confirming the results of Cournand et al.[65] In patients with normal or slightly impaired circulatory reactions elevation of mean mask pressure had only a temporary effect on cardiac output and arterial pressure. In the presence of shock or vasomotor paralysis there was a close correlation between circulation impairment and elevation of mean mask pressure. Price, Conner and Dripps,[66] using arterial pressure as the principal criterion, found that anesthetized patients seldom had normal circulatory reactions to pressure breathing and that circulatory impairment was proportional to elevation of mean mask pressure in patients who had greatly reduced vasomotor reactivity. They also found that the circulatory effects of positive-negative devices were disappointing; the negative pressure phase was usually too short to have much effect, and the mean mask pressure was well above atmospheric. When they created a subatmospheric mean mask pressure by a special apparatus the arterial pressure was increased. These results are consistent with those previously reported by others,[67-70] except for their finding that positive-negative-pressure respirators often did not have an effective negative phase.

The practical significance of the physiologic differences between positive-negative and fluctuating positive-pressure respirators is not known, since there is insufficient information on the circulatory responses of apneic patients; since many critically ill apneic patients have been treated with tank respirators and other forms of positive-pressure breathing for many hours, it is apparent that the detrimental effects of positive airway pressure should not be exaggerated. However, it should be pointed out that tank respirators have an expiratory intratank positive phase that corresponds to a negative phase in a mask respirator; the extent to which this phase minimizes circulatory impairment is not known.

The circulatory effects described are almost entirely related to the effects on venous return, rather than to pulmonary capillary compression.[71] Such effects are therefore less apparent in thoracic surgery, in which some circulatory impairment occurs when the chest is opened and most of the external surface of the lung remains at atmospheric pressure when subsequent mechanical ventilation is induced. Thus, the possible circulatory benefit from a negative intrapulmonary pressure is unlikely when the chest is open; furthermore, the lung-collapsing effect of negative

intrapulmonary pressure is even greater with the chest open and contraindicates the use of a negative phase under these conditions.

In summary, the hemodynamic phenomena that accompany alterations of airway pressure are well established. Positive intrapulmonary pressure impairs venous return, ventricular outputs and arterial pressure; these functions are restored during expiration, when compensating mechanisms are normal. Increased negativity of intrapulmonary and intrapleural pressures promotes venous return, ventricular outputs and arterial pressures. In the presence of deficient circulatory compensation mechanisms impairment increases with increasing mean mask pressure and decreases with falling mean intrapleural pressure (as in normal breathing). Although the negative mask phase is of assistance in reducing circulatory impairment when it occurs, in practice most resuscitators of the positive-negative-pressure variety have so little negative phase that the mean mask pressure is well above atmospheric.

Other Types of Artificial Respiration

Bloxsom Positive-Pressure Air-Lock

This apparatus does not really provide artificial respiration but has created great interest among pediatricians and obstetricians and has been reported in the literature as a device for resuscitation of the newborn.

Bloxsom described the apparatus as consisting of a chamber in which uterine contractions could be imitated by means of fluctuation of pressure of an oxygen-enriched atmosphere.[72] Temperature regulation and other controls qualified the chamber as an incubator. In usual operation the level rose slowly from 1 pound per square inch to 3 pounds per square inch above atmospheric pressure and then fell more rapidly to the former level, completing the cycle. With a slow phase of forty-five seconds and a decompression phase of fifteen seconds, there was 1 cycle per minute, but the rate could be increased to 2 per minute. Several benefits were said to result from the cycling pressure, including an expulsive effect on secretions in the air passages. No evidence has yet appeared in the literature to substantiate the specific benefits claimed. Regarding its use as a resuscitator Apgar and Kreiselman[73] demonstrated that apneic animals could not survive in the chamber unless spontaneous breathing was present. Computations from known respiratory characteristics of newborn babies and density changes in the chamber indicate that less than 3 per cent of the ventilatory needs of the baby can be met by a rate of 1 cycle per minute. On this basis it appears wise to consider the device an incubator and not a resuscitator.

High-Mask-Pressure Devices

In 1952 Day et al.[74] suggested a novel way of inflating a collapsed neonatal lung. Noting that stress on the lungs related to the pressure difference between its inner and outer surfaces they reasoned that a high pressure could be applied safely to the trachea if the pressure did not endure long enough for intra-alveolar pressures to rise to the mask-pressure level. Bursts of high pressure could therefore be applied to intrabronchial obstructions without endangering the alveoli. The method appeared to deal successfully with unilateral atelectasis of excised lungs.

Conclusions

Significant progress has been made toward an understanding of the physiologic and biochemical events of acute respiratory failure. The tools are available to study the mechanical behavior of the lungs in these circumstances, although few opportunities for such study have occurred. By inference it is known that the lungs are likely to be inflated with difficulty, in part because of high air-flow resistance and often because of changes in elasticity or compliance owing to pulmonary edema and related pathologic changes. These observations emphasize the importance of establishing criteria of alveolar ventilation rates rather than depending on pressure measurements in the airway or in a tank respirator. The limits of safe pressure levels in the lungs are not precisely known.

Many methods of artificial respiration are capable of giving adequate ventilation of the lungs unless the airway is obstructed or the lungs are excessively uncompliant. Manual methods with an active inspiratory phase are much superior to those with only an active expiratory phase. Cuirasses that enclose the chest and abdomen and methods that rock the body through an arc of 60° or more at respiratory frequencies are less effective than other mechanical respirators but are very valuable for special purposes such as use during convalescence from respiratory poliomyelitis.

Mechanical respirators include the body-enclosing tank and the automatically cycling devices that bring about changes in pulmonary air pressure through application to the face or endotracheal tube. Physiologically, the two types have the same respiratory and circulatory effects, since in either case the pulmonary pressure on inspiration is elevated above pressure surrounding the body.

The respiratory effects of artificial respiration do not appear to be materially different from those of naturally induced respiratory movements. However, few measurements of ventilation distribution, diffusion capacity and ventilation-perfusion relations have been made. As in all forms of external respiration, an effective active inspiratory phase appears to be of prime importance.

The circulatory effects of artificial respiration encompass a spectrum from the circulation-promoting action of natural respiration to the potentially severe impairment that may be due to a fluctuating positive-pressure device. The circulatory reserves of the patient are of paramount importance. If circulating blood volume is reduced, or if vasomotor reactivity is

diminished by anesthetic agents, other drugs or shock the effect of a high mean mask pressure is to lower venous return and thus to reduce cardiac output and arterial pressure. These effects are only temporary in patients with normal circulatory reserve mechanisms. In the impaired patient the results can be serious, but deleterious consequences can be minimized by general supportive measures and reduction of the mean mask pressure. The success of any method of artificial respiration is favored by knowledge of the underlying physiologic mechanisms and their interactions with the methods used.

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MEDICAL INTELLIGENCE

CHLORPROMAZINE IN PATIENTS WITH NAUSEA AND VOMITING DUE TO ADVANCED CANCER*

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NAUSEA and vomiting are frequent and annoying complications seen in a large proportion of patients with advanced and incurable cancer. In these patients it is often impossible to alleviate nausea or vomiting, except when it is due to mechanical causes that can be corrected by palliative surgery or temporarily remedied by various conservative mechanical means. In many cases either the mechanism is unknown or the cause is inaccessible to surgery, as in inoperable brain metastases.

Studies by others[1-3] have shown that chlorpromazine hydrochloride§ was effective in suppressing nausea and vomiting caused by a wide variety of clinical conditions, including carcinomatosis. It has also been shown that the drug does not have any serious toxic effects in man. It seemed, therefore, of interest to conduct controlled clinical studies for the purpose of determining the possible usefulness of chlorpromazine in the management of patients with terminal cancer plagued by nausea and vomiting.

Plan of Study

The patients were unselected except for the fact that they had advanced cancer and were suffering from nausea and vomiting. During the period of this study, all patients with cancer at the Holy Ghost Hospital fulfilling these criteria were given chlorpromazine in tablet form, 25 mg., two to four times a day, for varying periods up to three weeks without interruption. In some cases the drug was given in repeated courses spread over periods up to four months. Occasionally, when there was severe vomiting, some of the first doses were given by intramuscular injec-

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§Kindly supplied as Thorazine for investigational use by Smith, Kline and French Laboratories, Philadelphia.

tion. When improvement had occurred, placebo tablets were substituted periodically to determine whether the observed effects were real or psychologic. An effort was made to keep all other medication and the daily hospital routine as constant as possible throughout the clinical trial.

The severity of nausea was graded more or less arbitrarily, according to the patient's statements. In interviews with patients an attempt was made not to ask suggestive or leading questions, but rather to await their spontaneous statements. Placebo effect was balanced by the fact that the patients did not know the exact purpose of the medication.

The severity of vomiting was graded according to the number of times a day that vomiting occurred, regardless of the type or amount of nourishment taken. Thus, vomiting occurring three to five times a day was graded as "mild," that occurring six times a day as "severe," and that occurring seven or more times a day as "very severe."

Results

The analysis of results in 20 patients, from forty-four to eighty-five years of age, with cancer of the breast (8), cervix (1), pancreas (1), gastrointestinal tract (4), ovary (1), brain (1) and lung (1) or leiomyosarcoma (1) or multiple myeloma (2) showed that all of those with mild vomiting experienced complete relief after the administration of chlorpromazine (9); in 6 of 9 patients with severe vomiting complete relief followed therapy, and in 3 the vomiting was reduced in frequency. Of 2 patients who had very severe vomiting 1 stopped vomiting, and in the other the frequency was reduced.

One of these 20 patients had no nausea but only vomiting. In the remaining 19 with varying degrees of nausea this was eliminated in 11 and diminished in 6. In 2 patients no evaluation of the therapeutic effect of chlorpromazine on nausea was possible because they were too ill to give reliable reports on nausea.

Selected case histories are given below.

It is evident that in all cases — regardless of the cause of nausea and vomiting, and of the extent and stage of the carcinomatosis — improvement or complete control of nausea and vomiting was obtained whenever chlorpromazine could be given for a sufficient time. It is quite certain that the effects observed were true drug actions. In every case in which placebos were substituted symptoms of nausea and vomiting recurred promptly, but were once again relieved when chlorpromazine medication was resumed. The uniformity of favorable results suggests that a high rate of successful responses may be expected from the use of the drug as an antiemetic in cancer patients, and justifies the conclusion that it is a valuable agent for the relief of vomiting and nausea in patients with advanced, incurable cancer.

Side Effects

The undesirable side effects observed were occasional drowsiness and dryness of the mouth. These could be alleviated by a reduction in dosage. All patients received opiates for their pains, and this, of course, contributed to the development of drowsiness.

In 1 patient a skin rash appeared during therapy and disappeared on withdrawal. Oddly enough, the rash did not recur when chlorpromazine treatment was resumed, so that it was not possible to determine whether this skin reaction was related to the therapy.

Another patient, a sixty-eight-year-old woman with widespread cancer of the breast who was placed on treatment after this series had been completed, became depressed and emotionally unstable, and had frequent crying spells; before therapy this patient had already been somewhat emotionally labile. Winkelman[4] recently reported that symptoms in some agitated senile patients may be aggravated when chlorpromazine is first given, but later are well controlled as therapy is continued. This might be kept in mind when one attempts to control nausea and vomiting in elderly and debilitated patients with cancer, who often have varying degrees of mental disturbances. And, in depressed patients, the drug, like other sedatives, should be used with care and withdrawn if the depression deepens.

Case Reports

Case 1. W.H., a 52-year-old woman, was admitted to the hospital because of an inoperable carcinoma of the cervix. Examination revealed that the carcinoma had infiltrated the pelvis without, however, compressing the ureters. Three months later the patient began to vomit, usually 4 to 6 times a day. Laboratory studies disclosed an elevated blood urea nitrogen.

When 25 mg. of chlorpromazine was given by mouth, 3 times a day, vomiting ceased within 24 hours. The patient then resumed a regular hospital diet. Ten days later the drug was discontinued, and nausea and vomiting recurred within 1 week. Once more nausea and vomiting ceased when chlorpromazine was given in the same dosage as before, 75 mg. a day; it later was reduced to 25 mg. twice a day because of drowsiness. For 2 months the patient took 50 mg. daily without recurrence of nausea or vomiting. The blood urea nitrogen remained stationary. At the end of 2 months the drug was discontinued, and within 24 hours vomiting recurred.

At this time she received 25 mg. a day by mouth, with immediate cessation of emesis. Twenty-five days later a placebo preparation was substituted. Forty-eight hours later she again began vomiting 4 to 6 times a day. Therapy was resumed, and no vomiting occurred until she died of uremia 6 weeks later.

Case 14. E.K., a 65-year-old woman, was admitted to the hospital because of widely disseminated multiple myeloma. Examination and laboratory studies disclosed edema, massive albuminuria and an elevated blood urea nitrogen. On the 4th hospital day nausea and vomiting began, emesis occurring 4 or 5 times daily. When 25 mg. of chlorpromazine was given 4 times a day vomiting and nausea ceased promptly. Twelve days later placebos were substituted, and vomiting recurred at the same rate as before medication. The patient continued to vomit intermittently for 10 days until the drug was resumed at a dosage level of 100 mg. daily. Vomiting ceased on the 2d day of therapy. After 10 days a placebo was once more substituted, with prompt resumption of vomiting. Chlorpromazine was again given, and no nausea or emesis recurred until death two weeks later.

A maculopapular skin rash developed 12 days after the 1st administration of chlorpromazine. When the drug was temporarily discontinued, the rash disappeared; when it was resumed, no skin lesion occurred during the remaining weeks of therapy.

CASE 12. A.H., a 55-year-old man, entered the hospital 31 days before death from an inoperable cancer of the lung with metastases to the brain. On the 12th hospital day severe and frequent vomiting began. He was given chlorpromazine, 25 mg., 4 times a day, but this had to be reduced to 25 mg. twice daily because of drowsiness. On this lower dosage he remained alert, and no vomiting occurred for the 11 days remaining before death.

CASE 3. M.G., a 53-year-old woman, entered the hospital because of brain metastases from a cancer of the breast. She survived for 5 months and was plagued by frequent vomiting from the beginning of her hospital stay. There was no nausea. Chlorpromazine, 25 mg. 4 times a day, was given, and vomiting ceased on the 2d day of therapy. On the 14th day of therapy placebos were substituted, and vomiting recurred in 2 days. Chlorpromazine therapy was resumed. For 4 months, until death, she was able to retain her food and only occasionally, toward the end of her life, did she vomit.

CASE 10. M.H., a 47-year-old woman, was admitted to the hospital with an inoperable recurrence of carcinoma of the large bowel. After 10 weeks in the hospital signs of intestinal obstruction appeared, and she vomited 4 or 5 times daily. She received 100 mg. of chlorpromazine a day, and vomiting stopped within 12 hours. There was no emesis for 4 days, when she died suddenly. Autopsy revealed peritonitis from a perforation at the site of the tumor.

CASE 16. A.I., an 85-year-old woman, entered the hospital 36 days before death from widely disseminated abdominal carcinomatosis, which originated from an adenocarcinoma of the ovary. She was vomiting 4 or 5 times a day. On chlorpromazine therapy vomiting was greatly reduced until the 22d day of hospitalization, when the abdomen became markedly distended and she regurgitated small amounts of a fetid fluid. Chlorpromazine therapy was continued, and vomiting was never more frequent than twice a day until death.

SUMMARY

Chlorpromazine produced prompt relief of nausea and vomiting of patients with advanced incurable cancer when given orally or intramuscularly. Emesis was controlled for as long as four months. The only side effects observed in 20 patients studied for this period were occasional drowsiness and dryness of the mouth.

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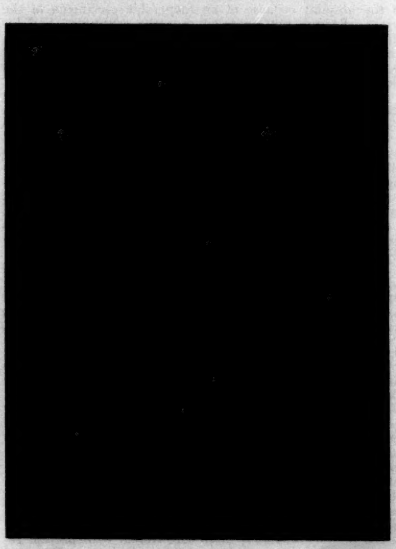

MASSACHUSETTS PHYSICIANS ART SOCIETY

32. *Bobbie Allen*

Second Prize, American Physicians Art Exhibit, 1944

Sculpture by

SIDNEY C. WIGGIN, M.D.

President, Massachusetts Physicians Art Society

CASE RECORDS
OF THE
MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

BENJAMIN CASTLEMAN, M.D., *Editor*

VIRGINIA W. TOWNE, *Assistant Editor*

CASE 40451

PRESENTATION OF CASE

A fifty-three-year-old man entered the hospital because of epigastric pain.

Twenty-five years previously, after he had immigrated to this country from Ireland, he began to have periodic episodes of epigastric pain, which occurred usually in the spring and fall and lasted for about three months. The pain radiated occasionally to the midback, was worse when he was hungry and was relieved by milk, cream and cereals. Gelusil and frequent feedings reduced the pain. Three years before admission the condition was investigated in another hospital. He was given Gelusil, Amphojel and a bland diet, and he remained symptom free for two years. During the past ten months the pain had recurred and was not relieved by diet and Gelusil. He had lost about 10 pounds in the past three years, but had gained 4 pounds in the last month. There was no history of melena, vomiting, hematemesis or abdominal distention. He had never had other ailments.

Physical examination revealed a man in no acute distress. The heart was normal. There were coarse inspiratory rales all over the chest. The epigastrium was slightly spastic and tender. There was no palpable mass. Rectal examination was negative. The prostate was soft, but slightly enlarged.

The temperature, pulse and respirations were normal; the blood pressure was 140 systolic, 75 diastolic.

Urinalysis was negative. The blood hemoglobin was 14.6 gm. per 100 cc., and the white-cell count 10,000, with a normal differential. The gastric analysis showed 13 units of free acid in the fasting specimen and 72 units half an hour after histamine; the guaiac test was negative. A roentgenogram of the chest demonstrated a few discrete calcifications in the right-midlung field. The heart, mediastinum, aorta, diaphragm and bones were normal. A gastrointestinal series revealed that the esophagus was normal; the gastric mucosal folds were tremendously enlarged (Fig. 1), and the stomach was irritable and hyperactive, with rapid emptying and deep peristaltic waves. The folds in the fundus of the stomach were so large that it was impossible to distend this area with barium, but the stomach seemed pliable throughout. The duodenal cap was persistently and markedly deformed and its mucosal folds were enlarged, but no definite crater was recognized.

On the second hospital day, an operation was performed.

FIGURE 1. *Film from the Gastrointestinal Series. The enormously enlarged folds on the greater curvature of the stomach are indicated by arrows.*

DIFFERENTIAL DIAGNOSIS

DR. EDWARD B. BENEDICT*: This fifty-three-year-old man had had for twenty-five years a fairly typical history of peptic ulcer, which I assume was duodenal not only because duodenal ulcer is more common than gastric ulcer but also because the x-ray films later showed a marked deformity of the duodenum. The history was typical of ulcer in that the pain occurred in the spring and the fall, and radiated to the back, which may mean that the ulcer was on the posterior wall; the pain was worse when he was hungry and was relieved by milk. The patient had lost 10 pounds in three years, which is not a very rapid loss of weight, and he had gained 4 pounds in the last month.

Something apparently had happened in the last ten months because the pain had not been relieved by diet and Gelusil. I am supposed to decide what happened in that period. The epigastrium was slightly spastic and tender; I do not think that is very significant because that can occur with an ulcer, gastritis or even a tumor. The normal temperature does not help

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me. The hemoglobin was normal, but it may be normal with an early tumor. The white-cell count and the gastric analysis are also of no help. Of course, a low acid content points toward a carcinoma but it would not be diagnostic. About the findings in the x-ray examination, I think I am supposed to decide what is meant by the tremendously enlarged mucosal folds, with irritability, hyperactivity and rapid emptying of the stomach at that time. The folds were said to be so large in the fundus that it was impossible to distend that area with barium. That really sounds important, but then the mucosa was said to be pliable throughout. I should not expect it to have been pliable throughout in tumor, so all I can say so far is that the patient had a duodenal ulcer.

The operation that was performed on the second hospital day may have been a gastroscopy; if so I probably should have done it myself or I should have heard about it. What could a gastroscopy have told us that we do not already know? In 1946, in a series of 245 patients in whom the diagnosis was proved by microscopical examination, an attempt was made to correlate gastroscopic, roentgenologic and pathological findings in diseases of the stomach, and it was concluded that greater diagnostic accuracy was attained when both x-ray and gastroscopic examinations were used co-operatively than when either method was used alone.[1] That is recognized in a recent article by Klotz, Kirsner and Palmer,[2] who analyzed 1382 gastroscopic and corresponding roentgenographic studies. They concluded that "a 30 per cent indecisive x-ray diagnosis of all cases in this series was reduced to 11 per cent by the additional examination of gastroscopy." About the thick folds specifically they say that "in 33 cases the incidence of indecisive diagnosis by radiology alone was 51.5 per cent," which is quite high. "Eighty-two per cent of those cases were correctly diagnosed by gastroscopy, 18 per cent incorrectly; the error by the combined procedures was 12 per cent." There is no rivalry between the two methods; each complements the other.

If a gastroscopy had been done, what information might have been added in this case? I have seen thick folds when they did not mean anything. The stomach can be distended with air at the time of gastroscopy and still appear normal. A biopsy from the folds may be reported negative by the pathologist. By gastroscopy one may be able to establish a diagnosis of gastritis, and the biopsy may show chronic gastritis or sometimes acute gastritis. Sometimes, even when the radiologist sees thick folds, the gastric mucosa to the gastroscopist may appear completely atrophic and smooth, with no folds at all. We must always consider lymphoma when the radiologist talks about thick folds, and a biopsy through the gastroscope sometimes, although not always, reveals lymphoma. If we take several samples and take them deep enough we should be able to make a positive diagnosis of lymphoma. Infiltrating cancer could have produced these folds, and gastroscopy should help make the diagnosis, especially if a biopsy is taken. To complete the subject of tumors I might mention sarcoma. Nothing in this case indicates a sarcoma. The x-ray films should have shown a filling defect and rigidity of the stomach if this type of tumor had been present.

I do not think a gastroscopy was done. The surgeons probably went ahead with a laparotomy, which I think was justified because the patient had a long-standing history of ulcer and also had recently failed to have symptomatic relief on good medical therapy. Furthermore, he had lost 10 pounds in weight, 4 of which he had regained.

What did the surgeons find? I think they found a duodenal ulcer and probably chronic gastritis. I do not believe there was tumor. The gastritis, which one always observes with a duodenal ulcer, is usually more antral; these thick folds were in the fundus of the stomach. I think the patient had diffuse chronic and perhaps acute gastritis, which may have given him the more severe recent symptoms.

I purposely delayed seeing the x-ray films, but I should like to see them now and reserve the right to change my opinion afterward.

DR. JOHN F. GIBBONS: The films demonstrate diffuse enlargement of the mucosal folds both in the stomach and in the duodenum. The air-contrast films bring out the huge size of the rugae; in this film, particularly, the great width of the folds is visible by coating of the greater curvature. There does not seem to be any localized constriction or filling defect in the stomach, and apparently the fluoroscopist could not see any rigidity. This film of the fundus with some barium in it does not give any evidence of a localized lesion. In other words, from the esophagogastric junction, apparently, to the antrum and through into the duodenum, the mucosa is heaped up into quite prominent folds. There is a deformity of the duodenal bulb, which never fills out adequately, and there is a constriction in the midportion. There is no evidence on the films of a localized ulcer crater in the duodenum or in the stomach. The stomach apparently empties very rapidly because in these films, which are usually made immediately after the fluoroscopic examination, the head of the barium column is already well down in the ileum. On this film there is evidence of marked peristaltic activity, with deep waves.

DR. BENEDICT: I think all that is consistent with duodenal ulcer and gastritis; although I am impressed with the thick folds, I think I shall stick to my diagnosis.

DR. ALLEN G. BRAILEY: Does the patient not seem to have a small amount of free hydrochloric acid? Does that bother you at all?

DR. BENEDICT: It does not bother me too much: he had a fairly good response to histamine.

DR. BENJAMIN CASTLEMAN: Dr. Kleaveland, would you tell us the preoperative diagnosis?

DR. RICHARD N. KLEAVELAND: I believe that Dr.

Claude E. Welch, like the radiologists, thought that this patient had a chronic duodenal ulcer with an element of gastritis.

At the time of operation we were quite surprised to see what appeared to be a large, diffusely edematous stomach. The whole stomach from the cardia down to the duodenum was very thick and had a certain translucency to it. If one picked up the stomach in one's hand, it was about 1.5 cm. thick. Beneath the fingers, one could feel multiple mucosal rugae that were enlarged, and the stomach felt as though it were full of worms. A subtotal gastrectomy was performed.

DR. CASTLEMAN: Do you have any further comment, Dr. Benedict, before I show you the stomach?

DR. BENEDICT: I do not think I can add anything.

CLINICAL DIAGNOSES

Duodenal ulcer.
Gastritis.

DR. EDWARD B. BENEDICT'S DIAGNOSES

Duodenal ulcer.
Gastritis.

ANATOMICAL DIAGNOSES

Mucosal hypertrophy of stomach.
(Duodenal ulcer.)
Chronic gastritis, antral.
Chronic lymphadenitis, gastric.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: This picture of the stomach shows the "worms" that the surgeons felt through the stomach wall (Fig. 2). These were very large, somewhat edematous but fairly firm rugal folds. The rugae were not as large in the lesser curvature as they were along the greater curvature. The antrum was the only part of the stomach that was free of the large rugal folds. This gross picture could have been caused by one of several conditions described by Dr. Benedict — marked gastritis, lymphoma or carcinoma. If lymphoma or carcinoma had been present these folds probably would not have flattened on pressure. We tried this here; some disappeared, but most of them remained. Having had the opportunity to see one other case like this,[3] we thought it fitted in with the picture that was described in 1888 by Menetrier[4] as an example of mucosal hypertrophy of the stomach. These rugal folds have been likened to the convolutions of the brain. This condition is different from polyposis of the stomach, in which each polyp has an individual stalk; here the entire mucosa is corrugated without any stalks (Fig. 3). It is not associated with gastritis and does not go on to carcinoma. Microscopically, the mucosa shows a marked increase both in size and in the number of glands. Goodale and Sniffen,[3] from this laboratory, reported a case last year, and there was a more recent paper from the Mayo Clinic[5] in which 20 cases were collected; the authors concluded that this is not a precancerous lesion. A section through the antrum in the case under discussion showed gastritis of the type that we see with duodenal ulcer. Although a small piece of the

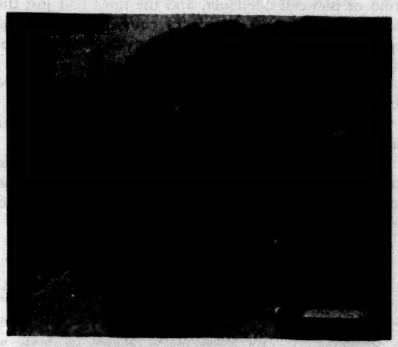

FIGURE 2.

duodenum was removed we were unable to find an ulcer in it, but I think the patient probably had duodenal ulcer, with antral gastritis that was quite different from the rest of the mucosa.

One interesting finding reported by the Mayo Clinic group is the high frequency of a low serum protein in these cases. Of their 20 patients 5 had a low serum protein — about 4 or 5 gm. per 100 cc. In 1 case the value returned to normal after gastrectomy.

FIGURE 3.

It is possible that if at operation the surgeons had taken out a piece of tissue and requested a frozen section a less extensive operation could have been done. In many cases total gastrectomies have been done because grossly this may appear to be diffuse carcinoma of the stomach. In this particular case the inflammatory reaction was so slight that I believe we might have been able to rule out gastritis, lymphoma and cancer.

DR. BENEDICT: I think that operation was justified. The process in the duodenum was definitely inflammatory and was quite different from the process in the stomach.

DR. CASTLEMAN: One other comment: 3 of the patients in the Mayo Clinic series had two endocrine tumors; 2 had pituitary tumors and either a parathyroid or islet-cell adenoma, and the third had just the latter two adenomas. This, of course, brings up the question whether this condition may have some endocrine basis.

DR. JACOB C. LERMAN: Acromegalic persons have large stomachs. Do they have this condition at all?

DR. CASTLEMAN: There is no mention of whether any of the patients were acromegalic.

DR. FAIRFIELD GOODALE, JR.: From a diagnostic point of view all these lesions usually occur on the greater curvature, and most of these patients also tend to have hypoacidity.

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CASE 40452

PRESENTATION OF CASE

First admission. A seventy-five-year-old man was referred to this hospital for study. Except for nocturia (two to three times) for many years he had been in good general health until four weeks previously, when fever and malaise developed and he experienced backache, urinary urgency and frequency and transient incontinence. Physical examination was said to have shown slight costovertebral-angle tenderness; the urine was loaded with white cells. He was treated with sulfadiazine and later penicillin, with improvement. The symptoms returned ten days before admission. Two years previously he had had a dorsal slit of the prepuce for stricture of the meatus.

Physical examination revealed a well developed, obese elderly man in no acute distress. The examination was negative except for a large irreducible right inguinal hernia, which retracted the penis. The urethral meatus was narrowed.

The temperature, pulse and respirations were normal; the blood pressure was 160 systolic, 85 diastolic.

The urine had a specific gravity of 1.004 and gave a ++ test for albumin; the sediment contained 10 red cells and 50 to 75 white cells per high-power field, the latter often in large clumps. Routine blood studies and blood chemical determinations were normal.

In an intravenous pyelogram the left kidney was large but normal in shape and position. The dye was excreted by the left kidney, outlining probably normal urinary passages. Overlying the upper half of the right kidney and extending upward from it was a round soft-tissue mass, 14 cm. in diameter, which seemed to change slightly in relation to the kidney. No definite dye was excreted in the lower half of the right kidney, but in the upper pole the upper calyx was visualized. Left retrograde pyelography was negative, and attempts on the right side were unsuccessful. Roentgenograms of the chest and gall bladder were normal; a barium-enema examination was incomplete because of the hernia. Peritoneoscopy failed to visualize the tumor so that it was thought to be retroperitoneal.

Meatotomy relieved the patient's complaints, and he was discharged after two weeks when he refused exploration.

Second admission (seven years later). He was admitted to the hospital because of recurrent "boring" pain in the right side and back for the last nine months. The pain was not related to meals but seemed to grow worse with constipation. There was no history of melena. Urinary symptoms included nocturia, slight hesitancy and dribbling. No history of hematuria or gravel in the urine was elicited. Five weeks previously an intravenous pyelogram was said to have shown a "cyst on the kidney." The patient had undergone herniorrhaphy a year previously in another hospital.

On physical examination a round mass was palpated in the right side of the abdomen.

The temperature, pulse and respirations were normal; the blood pressure was 140 systolic, 90 diastolic.

Urinalysis, after cystoscopy, showed a specific gravity of 1.010, with a + test for albumin and 60 red cells and occasional white cells per high-power field in the sediment. Examination of the blood revealed a hemoglobin of 12.2 gm. per 100 cc. and a white-cell count of 6800. The serum nonprotein nitrogen was 36 mg. per 100 cc. Other blood chemical determinations were normal. A retrograde pyelogram disclosed marked distortion of the superior calyceal system of the right kidney and a large mass in this region that had enlarged in comparison with its size in previous x-ray films. A barium-enema examination was negative. An intravenous pyelogram showed diminished function of both kidneys. The calyxes of the right kidney were displaced medially, and the entire kidney inferiorly. An electrocardiogram revealed atrial fibrillation.

Because of the age of the patient and the finding that the mass had not increased very much in size in seven years and because complaints were minimal, surgery was decided against, and he was discharged after three days.

Third admission (about nine months later). He was admitted to the hospital because of back pain radiating to the groin, right hip and down to the

right knee. The pain had become so severe during the past three months that codeine and Demerol had been required, and he had lost about 15 pounds in weight. There had been no nausea, vomiting, diarrhea, melena or jaundice.

Physical examination revealed a few rales in both bases. The heart was enlarged, and there was a Grade 1 apical systolic murmur. There was a football-sized tense, questionably cystic mass in the right upper quadrant that did not move on respiration. The liver edge was felt 2 fingerbreadths below the right costal margin.

The temperature, pulse, respirations and blood pressure were normal.

Urinalysis, routine blood and blood chemical studies were negative.

A neurosurgical consultant found pain distributed along the second and third lumbar dermatomes of the right thigh and hip. There was no sensory deficit or loss of muscle strength. X-ray films of the chest, spine, pelvis and skull were normal. A right retrograde pyelogram demonstrated a large mass in the right upper quadrant that displaced the kidney inferiorly and changed its axis. The upper pole of the kidney was not seen, and there was calcification in the inferior border of the mass (Fig. 1). The inferior and middle calyxes were spread by the mass. There was a suggestion of erosion of the body of the first lumbar vertebra.

On the eleventh hospital day an operation was performed.

Differential Diagnosis

Dr. Richard Chute*: May I look at the x-ray films, Dr. Hanelin?

Dr. Joseph Hanelin: The first examination, made seven years earlier, shows a smoothly rounded, roughly 7-cm. mass in the right upper part of the abdomen. I cannot distinguish the renal outline on that side, nor is it too clearly shown on the left side. An intravenous urogram taken at that time discloses function of both kidneys, with partial filling of the calyceal system on the right. The retrograde pyelogram demonstrates the ureter to be displaced downward and somewhat laterally on the right, but there is no opaque medium in the calyxes themselves. The left side is perfectly normal.

Dr. Chute: What do you think of the bladder?

Dr. Hanelin: It is asymmetrical and leans toward the left side for some reason.

A Physician: The patient had a hernia.

Dr. Hanelin: Seven years later a retrograde examination shows that the mass in the right upper portion of the abdomen has greatly increased in size and more than doubled in volume and that the calyxes are elongated and displaced downward and medially (Fig. 1). I am unable to separate the mass from the renal shadow. The intravenous urogram, done after the retrograde studies, reveals function preserved in both kidneys. Linear calcification is visible at the lower edge of the mass in the last two examinations done nine months apart. The mass has changed little in size in this interval. I cannot see any evidence in the spine of bone destruction. Degenerative arthritic changes are present.

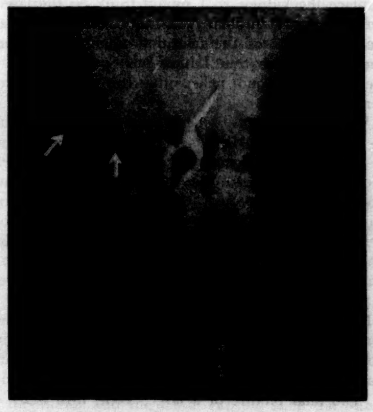

Figure 1. *Retrograde Pyelogram.*

Arrows point to the large mass in the right upper abdomen, which causes distortion of the calyxes and displacement of the kidney downward and medially. There is a small rim of calcification in the inferior aspect of the mass.

Dr. Chute: When one sees the x-ray films, the situation always looks different from the way one has figured it out on paper. The question is, What was this mass that was displacing and deforming the right kidney? It looks to me as if the kidney were more displaced than deformed. What are the pathological possibilities in this region? Let us first consider diseases of the intraperitoneal organs in this area: the liver, gall bladder, common duct, duodenum, colon, mesentery, omentum and for practical purposes the pancreas, although the pancreas is really retroperitoneal. The lesion was first observed nine years and nine months previously as a round cantaloupe-sized mass, which to me suggests either a cyst or a tumor. If it had been a malignant lesion of the liver, gall bladder, common duct or pancreas, the x-ray film of the gall bladder would probably not have been normal, and there would have been digestive symptoms, jaundice and, above all, a much more rapid course. Cancer of the colon would have had a more rapid course, with obstructive symptoms, and would not have given a negative barium-enema examination. Hydrops of the gall bladder has been known to dis-

*Member, Board of Consultation (formerly, visiting urologist), Massachusetts General Hospital; chief, Urological Service, Veterans Administration Hospital, Boston.

place the right kidney, but the x-ray films of the gall bladder were normal. A cyst of the liver is a possibility but seems unlikely to me, as do cysts of the omentum or mesentery. Echinococcus cyst has to be considered in passing. We do not know where the patient was born, but calcification at the lower border of the mass was not observed until the last admission, and no shadows suggestive of daughter cysts were mentioned. Schulte and Emmett[1] have shown that even quite large cysts of the pancreas usually do not displace the kidney, so I should think on the law of averages that it probably was not a cyst of the pancreas. In view of the fact that none of the intraperitoneal lesions that I have mentioned seem to fit the picture, I do not believe that this mass was intraperitoneal.

What are the possibilities of a retroperitoneal mass — a lesion of the kidney or adrenal gland, or one of the tumors that occur in the retroperitoneal area? Most of the retroperitoneal tumors are malignant and would not be expected to run such a long course. Furthermore, they usually do not start as an obvious round mass, but are more irregular and infiltrative. Therefore, I shall vote against retroperitoneal tumors, which leaves only the adrenal glands and kidneys as probable sites.

I may be getting ahead of myself, but I believe that the lesion first observed nine years and nine months previously was benign, probably a cyst, and that later a malignant tumor arose in connection with it. The final picture of a large, fixed, firm mass, of intractable pain in the back referred to the groin, hip and knee, with possible erosion of a lumbar vertebra, and of 15 pounds' weight loss suggests a malignant lesion to me.

A cyst of the adrenal gland is a possibility, but adrenal cysts are not common and renal cysts are. Malignant tumors of the adrenal cortex are commoner than those of the medulla and are usually adenocarcinoma. These may or may not function in a hormonal fashion. In this elderly man there was no hint of feminization. Adenocarcinomas of the adrenal cortex are usually not large, whereas kidney tumors frequently are, and metastasize rapidly via the blood stream, as well as locally, and this patient did not show generalized metastases. Neuroblastoma is a very malignant tumor of the adrenal medulla but usually occurs in young children and is very rare in the aged. Ganglioneuroma is a possibility; it is considered benign, but it has malignant potentialities. There is nothing about the case to suggest pheochromocytoma. Metastases to the adrenal glands are commoner than all the primary adrenal growths put together and are a possibility, but this case does not strike me as that.

A renal tumor arising in association with a renal cyst appeals to me more than adrenal disease. A benign adenoma of the kidney, which later became malignant, is a possibility although I am surprised that there were no red cells in the urine. I think that during these years the patient had a renal cyst, which naturally did not connect with the kidney pelvis, and that finally a malignant renal tumor developed inside the cyst, which was the reason that the urine did not contain red cells. If I were asked to give a second choice, I should say that he had had a renal cyst and that a metastasis from somewhere to the adrenal gland accounted for the final picture.

DR. WINFIELD S. MORGAN: Would you like to pinpoint the type of cyst, Dr. Chute?

DR. CHUTE: I think it was a large, simple cyst. Could you tell whether it moved with the kidney, Dr. Hanelin?

DR. HANELIN: I do not know whether it did or not.

DR. CHUTE: In association with this type of cyst various types of kidney tumor may develop — most commonly papillary cystadenoma or adenocarcinoma. I should guess that this was a large renal-cell carcinoma.

DR. HOWARD ULFELDER: Could this have been an aneurysm of the renal artery?

DR. CHUTE: I should not think so, but that is a good point. Calcification can occur in both renal cysts and renal tumors, and also in aneurysms of the renal artery, where the calcification that is commonly seen is a ring-shaped shadow, which I have happened to see only on the left side.

DR. FREDERICK G. SHAFFER: This patient was referred to us by the Orthopedic Service, where he entered because his primary complaint was hip pain. At urologic rounds, opinions were varied. Most of us thought he had a cyst of the kidney. He was an extremely obese man, weighing almost 250 pounds. Some urologists advised putting a needle in the cyst to relieve the pressure on the nerves. However, it was decided to operate on him.

CLINICAL DIAGNOSIS

Renal tumor.

DR. RICHARD CHUTE'S DIAGNOSIS

Renal cyst, with renal-cell carcinoma.

ANATOMICAL DIAGNOSES

Renal-cell carcinoma, with cystification and with metastases to retroperitoneal region.
Renal cysts, multiple.
Nephrosclerosis.

PATHOLOGICAL DISCUSSION

DR. SHAFFER: When the kidney was exposed through an incision extending anteriorly from the tip of the twelfth rib, it was seen to be completely destroyed by a cyst that contained hemorrhagic material. Accordingly, it was decided that nothing could be salvaged and that the kidney should be removed

without opening the cyst. The twelfth rib was resected, and in removing the rib we ran into a tumor involving the first lumbar vertebra and the quadratus lumborum muscle. We thought that this might be a tumor of the sympathetic chain, and frozen section of the tumor indicated that it was consistent with a paraganglioma. However, it was later proved to be not so. We removed the tumor from the lumbar vertebra, resected a large part of the quadratus lumborum muscle and removed the kidney entirely. Postoperatively, the patient did extremely well; however, he continued to complain of extreme pain in the right hip. We gave him a short course of x-ray treatment to relieve the pain in the left hip, with dramatic success.

DR. MORGAN: The specimen we received in the laboratory consisted of a large, previously opened cystic mass which had replaced the upper pole of the kidney (Fig. 2). The cyst was sharply demarcated from the adjacent normal renal parenchyma, and its wall was tough, fibrous and continuous with the capsule of the kidney. The contents of the cyst consisted largely of chocolate-brown, hemorrhagic and necrotic material. Also submitted was a mass of tumor from the retroperitoneal region. The remaining kidney showed numerous thin-walled cysts of the retention type measuring from 0.5 cm. to 5 cm. in diameter.

Microscopical examination disclosed that this was a cystic carcinoma of the kidney, which had extended through the capsule to invade the retroperitoneal tissues. Portions of the tumor were of the clear-cell, others of the dark-cell and still others of the papillary type. Admixed with the tumor was a great deal of blood clot of variable age, and there was acute inflammation, with extensive necrosis.

Did this tumor develop relatively recently in a simple or retention type of cyst that had been present for years, or was it a cystadenocarcinomatous lesion from the beginning? Had this tumor been present for at least eight years, as indicated by the mass palpated during the first admission?

I do not believe that this tumor originated in a simple cyst; the wall of such a cyst is characteristically thin, translucent and smooth surfaced, and the capsule about this tumor was thick and hyalinized. On the other hand this was certainly quite different from the usual renal-cell carcinoma, which does not have a capsule of this dimension and is not so nicely demarcated from the adjacent kidney. The best classification for this tumor, I believe, is that of papillary cystadenocarcinoma. In this type of lesion the growth is inward into the cyst, with gradual stretching of the capsule, and probably only relatively late, except in extremely malignant tumors, is there extension or break through the capsule. I am reasonably certain that this tumor had been present for some time before the first admission, and this conclusion is in line with the nature of the lesion since the inward growth

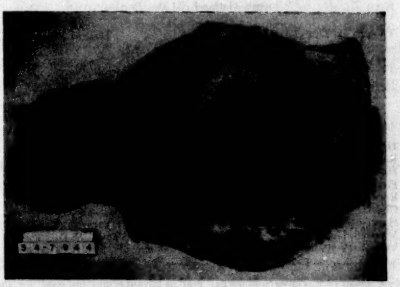

FIGURE 2.

of the tumor and the dense capsule keep the tumor from extending into radicles of the renal vein with subsequent metastasis, as is so frequently the case in renal-cell carcinoma, which, as is well known, need not be very large before metastasis occurs.

One of the most detailed studies of renal tumors is that by Melicow[2]; in his series of 199 tumors of the kidney there were 10 similar to the one under discussion. Of these, 4 were papillary cystadenomas, and 6 papillary cystadenocarcinomas.

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2. Melicow, M. M. Classification of renal neoplasms: clinical and pathological study based on 199 cases. *J. Urol.* 51:333-385, 1944.

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"PLACE OF NEW LIFE"

THE greatest problem that today faces the world's estimated 10,000,000 sufferers from leprosy is the social one, arising from the apparent ancient prevalence of the disease, the occasional conspicuousness of its lesions, its incurability prior to the discovery of modern methods of treatment and the fantastic misconception of its communicability. In this one respect cancer, the control of which has been developing so slowly compared with that of Hansen's disease, has never been greatly dreaded even by the most ignorant, and the great epidemic scourges were scarcely rated as any more highly contagious than leprosy.

From earliest recorded times the leper has been an outcast, tales of the punishment inflicted on him even today constituting a sinister anthology of physical and mental brutality. In no way reflecting a change in attitude — rather, in fact, confirming it — is the federal law rendering a person who stigmatizes another as a "leper" subject to fine or imprisonment. Such has been the general attitude of the world since Moses and Aaron were instructed in the identification of the leper who, named as unclean, was to make his habitation without the camp.

Always, however, there have been those willing to go among the lepers and devote their lives to their care, and gradually the attitude has been changing, particularly since the disease became curable. The leprosarium at Carville, Louisiana, capable of caring for 400 patients, — or approximately a quarter of those in the country, — is perhaps the most modern institution of its kind. Nursing care in this hospital, established by the state of Louisiana in 1894, is still, as it has been almost from the beginning, given by sisters of the order of Saint Vincent de Paul. The institution was purchased by the federal Government in 1921 and is now operated by the United States Public Health Service.

Other countries are also playing their part in removing the stigma from leprosy and in helping to prepare the way for a return of its victims to society. At Vellore, India, under the impetus supplied by the young British orthopedic surgeon, Paul W. Brand, the first leprosy rehabilitation center in the world has been established. It is appropriately named Neva Jeeve Nilyam, or Place of New Life.

Not only is excellent medical care now available for many lepers, but constructive efforts are being made for their economic and social rehabilitation, both directly and through the education of the public. Various church and social organizations are participating in this reform; prominent among them is the American Leprosy Mission, an outgrowth, established in 1906, of a Protestant society formed in Dublin in 1874, which became the Mission to Lepers, of Edinburgh and later of London, with branches in Canada, Australia and New Zealand. Its broad purpose "to help free the world from leprosy" is directed specifically toward furnishing "medical and surgical treat-

ment, spiritual care and social rehabilitation to men, women and children with leprosy." Thus are the afflicted being returned to life from the tombs in the Vale of Hinnom.

STILL A WORTHY ENTERPRISE

THE *Boston Post*, a morning newspaper, published on October 27 a brief story about the recently opened Lemuel Shattuck Hospital at Forest Hills, described in this column last week. The main features of the report were the cost of the hospital to the Commonwealth — $16,200,000; the number of persons employed to run it — 250 doctors, nurses, attendants and other employees at a weekly payroll of $15,800; the *ultimate* capacity of the hospital — 600 beds; and the fact that only twenty-three days after its doors were opened 31 patients, carefully selected as suitable beneficiaries of its unique services, had already been admitted.

It is unfortunate that the *Post*, despite its information having been derived from an interview with those in authority at the hospital, seems to have missed the true significance of the establishment of the institution. For the newspaper, treating this profoundly important and far-reaching development in the intelligent care of the Commonwealth's chronically ill citizens almost as if it were suitable material for party politicking, seems to imply that both the Legislature and the City Council had been hoodwinked by persons unnamed.

The *Post*, regrettably failing in this instance to grasp the principle of the greatest good to the greatest number seems to visualize the proper function of the Lemuel Shattuck Hospital as that of a sort of glorified almshouse where the incurably sick can end their days in what comfort their condition will permit. It is unfortunate that the imagination of the *Post's* reporter could not have been fired to see in the establishment of the hospital the means of studying chronic disease, of finding new and better methods of rehabilitation of the disabled and of training physicians, nurses, technicians and attendants in this important but neglected phase of medical care.

COTTON MATHER AND AMERICAN MEDICINE

THE distinguished Congregationalist divine of the early eighteenth century in Boston has been and still is a controversial figure in the history of America. Like a sponge, Cotton Mather constantly soaked up by extensive reading quantities of both theology and science, only to squeeze out from himself over a long period of years large and small drops in the form of pamphlets and books. In the field of medicine, in which he felt qualified by his reading, although without a formal degree, some drops were clear and even sparkling; many were muddy with ancient humoral silt, although always presented by Mather in a tight theological envelope. The best discoveries in nature, culled from his vast reading and correspondence, were set forth with religious enthusiasm, for Christianity encouraged his interest in science and Calvinism, as leavened by pietism, inspired his concern for social welfare. Like Franklin and Jefferson, he shared this dual orientation.

On medicine he wrote at length, but he usually seemed more learned than original, and more of a theorist than an observer. Yet Beall and Shryock* have found some remarkable exceptions to these generalizations. Oliver Wendell Holmes saw in Cotton's unpublished textbook of medicine, *The Angel of Bethesda*, the surviving anachronisms, the ramblings and moralizings, so glaring and obnoxious to his eye in 1869. Beneath them, however, in 1954, Beall and Shryock find a layer of balanced evaluation of science and a degree of selection of discrimination, with emphasis on discoveries of his time that later proved of major importance, such as his observations on hybrid corn and on immunization.

In inoculation for smallpox, during the epidemic of 1721, he certainly took a bold and unintimidated stand, backing up the young Zabdiel Boylston against William Douglass, the only Boston practitioner who held a medical degree. Mather aroused professional ire, but he never forsook his original intentions, though he was beset with doubts and fears, and the Boston experience of 1721 proved to be a major triumph for both Mather and Boylston. Mather, moreover, thought out a rational explanation for the phenomena of infection, both natural and artificial, and in *The Angel of Bethesda* he stated "that the Small-Pox may be more of an animalculated Business than we have been generally aware of." The animalculae (or "the contagion"), he surmised, entered the body through the respiratory passages, and so gained direct access to the blood and through it to vital organs. In other words, Mather held the view that the virus was probably composed of living organisms and that by inoculation into the skin it was in some way attenuated and thus caused a mild reaction.

Although Mather was not technically a physician, one can agree with Beall and Shryock that he was certainly the outstanding medical thinker as well as the moral leader throughout the epidemic of 1721 and that he rightfully emerges as the first significant figure in American medicine, in spite of being pinioned, in much that he wrote, by tight, binding pietism.

1955 PRIZE-ESSAY COMPETITION

ACCORDING to tradition, well established as traditions in America go, the *Journal* announces its seventh annual prize-essay competition open each year to

*Beall, O. T., Jr., and Shryock, R. H. *Cotton Mather: First significant figure in American medicine.* 241 pp. Baltimore: Johns Hopkins Press, 1954.

fourth-year medical students in schools approved by the Council on Medical Education and Hospitals of the American Medical Association.

As in previous years, the essay will consist of the report of a clinical case personally studied by the essayist, combined with a discussion of the pathologic condition represented by the case and a review of the important literature on the subject. The paper should follow the usual form of case reports as published in the *Journal*. Thus, the participant in competing for a substantial prize will do so not as a matter of supererogation but in the ordinary course of his or her academic obligations.

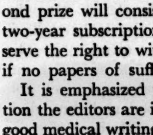
In detail, the competition requires that manuscripts be not more than 5000 words in length, clearly typewritten in English, double or triple spaced with references listed at the end in numerical arrangement according to the form used by the *Quarterly Cumulative Index Medicus*. They must be in the hands of the editor by March 15, 1955, and must be accompanied by a certification from the dean of the medical school concerned stating that the author is a member in good standing of the fourth-year class and specifying the expected date of graduation. No manuscripts will be returned.

A cash prize of $100 will be paid for the best essay of those found to be suitable for consideration, and the paper will be published in the *Journal* if the quality is considered to conform to the standards by which the editors usually judge material submitted; the author will receive a hundred free reprints. A second prize will consist of $25, and a third prize of a two-year subscription to the *Journal*. The editors reserve the right to withhold the awarding of any prizes if no papers of sufficient merit are submitted.

It is emphasized that in establishing this competition the editors are interested as much in encouraging good medical writing as in promoting the collection of scientific and clinical material. Particular attention will accordingly be paid to clarity, simplicity and general literary excellence.

Dr. Frey, a German medical pretender, is under arrest in New Jersey, for practicing by charms, instead of using real pills and powders.

Boston M. & S. J., *Nov. 15, 1854*



MASSACHUSETTS MEDICAL SOCIETY

DEATHS

BERGIN — Joseph David Bergin, M.D., of Worcester, died on October 7. He was in his fortieth year.

Dr. Bergin received his degree from Boston University School of Medicine in 1940. He was a member of the American Urological Association and the staffs of St. Vincent and Worcester City hospitals, and a councilor of the Massachusetts Medical Society.

He is survived by his widow, three sons, three brothers and a sister.

FULDER — Hans Fulder, M.D., of Worcester, died on October 11. He was in his forty-fifth year.

Dr. Fulder received his degree from the Université de Lausanne Faculté de Médecine in 1934. He was a member of the American Heart Association and the New England Heart Association and of the staffs of the Worcester City and Hahneman hospitals.

He is survived by his widow, three daughters, a brother and a sister.

McSHEEHY — Theobald C. McSheehy, of Worcester, died on October 14. He was in his eightieth year.

Dr. McSheehy received his degree from Columbia University College of Physicians and Surgeons in 1902. He was formerly a member of the staff of St. Vincent Hospital.

He is survived by his widow, four sons and four daughters.

UNIAC — Thomas V. Uniac, M.D., of Lawrence, died on October 8. He was in his seventy-fourth year.

Dr. Uniac received his degree from Dartmouth Medical School in 1909. He was a member of the staffs of the McGowan Memorial and Lawrence General hospitals and was formerly city physician for Lawrence and secretary of the Lawrence Medical Club.

He is survived by his widow and two sisters.

ZOVICKIAN — H. Hovhannes Zovickian, M.D., of Watertown, died on October 10. He was in his sixty-ninth year.

Dr. Zovickian received his degree from Harvard Medical School in 1917. He was a fellow of the American Medical Association and a councilor of the Massachusetts Medical Society.

He is survived by his widow, a son and a daughter.

BOSTON MEDICAL LIBRARY

HUNTER MEMORIAL FUND

The fund to establish a memorial within the Library to the late Dr. Francis T. Hunter, first announced in the October 7 issue of the *Journal*, had reached $1090 on October 28.

BOOK REVIEW

Atlas of Men: A guide for somatotyping the adult male at all ages. By William H. Sheldon, Ph.D., M.D. With the collaboration of C. Wesley Dupertuis, Ph.D., and Eugene McDermott, M.A. F°, cloth, 357 pp., with 5 illustrations and 19 tables. New York: Harper and Brothers, 1954. $10.00.

This is an important book. Its contribution is that of a scientific attempt to answer the question of whether or not a man's physical configuration is a measure of his ability, temperament and social pattern, and to some degree his susceptibility to certain diseases.

Dr. Sheldon's previous work in the definition of body types is represented by *The Varieties of Human Physique* (1940), *The Varieties of Temperament* (1949) and *Psychology and the Promethean Will*.

The history of efforts to place human shapes in easily delimited groups is a long one. What Sheldon and his asso-

ciates have added is the method of somatotyping in which all persons are divided into endomorphs (soft and round and related developmentally to the primitive gut), mesomorphs (muscular, rugged and related to the musculoskeletal system) and ectomorphs (linear, poorly muscled, with comparatively large ratio of surface area to mass, related to the ectoderm). However, pure types do not exist, and each of the 3 elements is further divided into seven gradations. Since each man consists of a fraction of roundness, muscularity and linearity his somatotype can be expressed by 3 numbers designating in this order the degree of these factors (each on a scale of 7), which he exhibits.

Four thousand college students were originally measured and photographed in 3 positions with a standard technic. The Constitution Project has developed so that this atlas is a report on the study of 46,000 men, and it has been possible to extend the sample into the older age groups. Nutritional alterations have been carefully considered to clarify the point brought up by some critics that the somatotype is merely a reflection of the nutritional status. There appears to be convincing evidence that the somatotype, itself, is immutable but that the genotype, the inherited factor, as affected by environment—that is, the phenotype—varies in relation to nutrition. The somatotype is defined "as a trajectory or pathway through which the living organism will travel under standard conditions of nutrition and in the absence of grossly disturbing pathology."

Other variables enter into somatotyping, such as the "r", or fineness factor; dysplasia, or inconsistencies between different body components; and gynandromorphy, or the female-male balance.

The major part of the volume is devoted to 1175 photographs of the characteristic somatotypes based on a rising preponderance of endomorphy from 1 to 7, with comparable variations in mesomorphy and ectomorphy. Thus, the range is from extreme leanness and lack of muscularity, through the "big muscle men," to the enormous, round, fat men with only Grade I linearity — that is, from the 117 type to the 741.

There is a certain fascinating whimsey in the author's description of these 88 different somatotypes. The 117 is the "walking stick." He is more prevalent in mental hospitals than in the general population, but also "encountered more frequently on college campuses, and there the diagnosis is sometimes *Phi Beta Kappa*." "Fours in the first component, of the 433 type," for example, are "sheep and deer, or whom the dogs hunt": "Delicate-limbed, fat bodied, inoffensive browsers whose personal deportment is usually above reproach except that they eat too much and are too easily influenced." "Sevens in the first component, of the 711 type" are "manatees and dugongs, the mermaids." All the 7's in endomorphy make up about 1 per cent of the male population.

The temperamental variants accompanying the respective somatotypes are in general those popularly attributed to them throughout the ages: the round, soft man loving comfort and companionship, the muscular dynamo seeking emotional outlet in physical-energy expenditure, and the slender ectomorph being sensitive and "cerebrotonic." Abnormalities in the mental sphere are shown to be linked to body type. For example, "Endopenes tend toward the paranoid reaction patterns."

The 343, 344, 353 and 443 make up 22.3 per cent of the male population. This is "the common man." The 343's are "airedales": "Spunky, ordinary fellows who physically are nothing in particular but who have good normal instincts and will gladly chase a rabbit or bark at a lion."

Many investigators have attempted to relate body shape to proneness to specific physical ills. There is considerable evidence that the muscular male who tends to put on fat is particularly vulnerable to diseases of the circulation. The 244, conversely, appears to be one of the half-dozen longest-lived somatotypes. The 252 is nearly always short but blessed with longevity, which suggests that "one prescription for long life may be contained in the formula: Short stature with sturdy mesomorphy which is not extreme mesomorphy." Many 254's have been observed with gastric ulcer: "People who get gastric ulcer, predominantly men, seem typically harder and leaner — more endopenic — than those who develop duodenal ulcer." The three very common causes of death for the 261 (note the increase in the muscular component) are apoplexy, renal failure, and acute coronary "accident." An observation of interest, but as yet unexplained, is that the 263 (in whom the linear, ectomorphic component is higher) is probably the longest lived of this "great-cat" type, and the 271 occasionally may be excessively long lived. The last is the "Hercules somatotype."

This volume is eminently readable and certainly inclines one to a deterministic point of view toward the permanence of the inherited structure. With the structure go, apparently, physical and mental assets and liabilities little influenced by environment. However, the author has shown that a great criminal and a great military genius may well have similar body shapes, and he is not unaware of the fact that he is painting with large brush strokes.

In spite of some dissenting voices, this reviewer believes that Sheldon's work will stand as a firm milestone on the alluring highway of medical anthropology.

HOWARD B. SPRAGUE, M.D.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Surgical Forum: Proceedings of the forum sessions, thirty-ninth clinical congress of the American College of Surgeons, Chicago, Illinois, October, 1953. 8°, cloth, 752 pp., with illustrations. Philadelphia: W. B. Saunders Company, 1954. $10.00.

There are nearly 400 papers in these proceedings. The subjects discussed include heart and great vessels; blood vessels and circulation; lungs; esophagus, stomach and intestine; liver and pancreas; burns and renal functions; shock, nutrition and electrolytes; wounds, infections, antibiotics and anesthesia; cancer and steroids; and plasma expanders. There are indexes of authors and subjects.

Annual Review of Medicine. Edited by Windsor C. Cutting, Stanford University School of Medicine; and Henry W. Newman, Stanford University School of Medicine. Vol. 5. 8°, cloth, 490 pp. Stanford, California: Annual Reviews, Incorporated, 1954. $7.00.

Twenty reviews by well known authorities in their particular fields are included in this volume. There is also an annotated list of reviews appearing in medical periodicals during 1953 and a list of articles to be published in 1955. There are indexes of authors and subjects, and all the articles have extensive lists of references. This is the type of serial that should be in all medical libraries.

NOTICES

HARVARD MEDICAL SOCIETY

A meeting of the Harvard Medical Society will be held in Amphitheater E, Department of Pharmacology, Harvard Medical School, on November 16 at 8:15 p.m. Otto Krayer will preside.

The program is as follows:

Mutation and Drug Resistance: A genetically unstable strain of *Escherichia coli*. Avram Goldstein.

An Experimental Approach to Behavioral Effects of Drugs. Peter B. Dews.

Synthesis of Steroid Alkaloids with Antiaccelerator Cardiac Activity. Frederick C. Uhle.

The Initial Rate of the Isolated Dog Heart and Its Response to Epinephrine. Joseph M. Benforado.

The Cardioaccelerator Action of Ephedrine and Its Use for the Quantitative Determination of Antiaccelerator Potency. Otto Krayer.

CHELSEA SOLDIERS' HOME

A professional staff meeting will be held in the Quigley Auditorium at the Soldiers' Home, Chelsea, on November 17, at 8:30 p.m.

Dr. Perry Culver, assistant physician, Massachusetts General Hospital, and associate in medicine, Harvard Medical School, will speak on the topic "Infectious Hepatitis." All physicians are invited.

ALPHA OMEGA ALPHA LECTURE

The first lecture sponsored by the Boston University Chapter of Alpha Omega Alpha will be delivered by Dr. Irving M. London, associate professor of medicine, Columbia University College of Physicians and Surgeons, on the subject "Metabolism of Hemoglobin and Bile Pigments," in the auditorium, Boston University School of Medicine, 80 East Concord Street, on November 22 at 5 p.m. The lecture is open to the medical profession.

MYASTHENIA GRAVIS FOUNDATION

A conference on myasthenia gravis, under the auspices of the Myasthenia Gravis Foundation, will be held at the School of Medicine, University of Pennsylvania, Philadelphia, on December 8 and 9. Physicians and students are invited. Further information may be obtained from the Myasthenia Gravis Foundation, 2 East 103d Street, New York 29, New York.

SOCIETY MEETINGS AND CONFERENCES

November, 1954–April, 1955. Postgraduate Medical Institute. Page 451, issue of September 9.

November, 1954–May, 1955. Sanitary Engineering Center Training Programs. Page 122, issue of July 15.

November 15. New England Cardiovascular Society. Page 793, issue of November 4.

November 15–19. American College of Surgeons. Page 496, issue of September 16.

November 15–26. Laboratory Diagnosis of Tuberculosis Course. Page 246, issue of August 5.

November 15, 1954–January 17, 1955. Hartford Medical Society. Page 496, issue of September 16.

November 16. South End Medical Club. Page 794, issue of November 4.

November 16. Harvard Medical Society. Page 833.

November 16 and 17. New England Diabetes Fair. Page 721, issue of October 21.

November 16–24. Consultation Clinics for Crippled Children in Massachusetts. Page 721, issue of October 21.

November 17. American Trudeau Society. Page 588, issue of September 30.

November 17. Massachusetts Academy of General Practice. Page 721, issue of October 21.

November 17. Industrial Medicine Symposium. Page 794, issue of November 4.

November 17. Chelsea Soldiers' Home. Notice above.

November 18. Nu Sigma Nu. Page 793, issue of November 4.

November 22. Alpha Omega Alpha Lecture. Notice above.

November 29–December 1. Association of Military Surgeons of the United States. Page 631, issue of October 7.

December 1, February 4 and April 8, Massachusetts Society for Research in Psychiatry. Page 679, issue of October 14.

December 3, 1954; February 4 and April 1, 1955. New England Society of Anesthesiologists. Page 1054, issue of June 17.

December 4, 1954–May 7, 1955. Middlesex South District Medical Society, Postgraduate Course. Page 758, issue of October 28.

December 5. American Academy of Dental Medicine. Page 1092, issue of June 24.

December 7. Medical Television Program. The Doctor. (Cavalcade of America.) Page 631, issue of October 7.

December 8. New England Pediatric Society. Page 968, issue of June 3.

December 8. Postgraduate Seminar in Psychiatry and Neurology. Page 452, issue of September 9.

December 8 and 9. Myasthenia Gravis Foundation Conference. Notice above.

December 13–17. Congress of Obstetrics and Gynecology. Page 748, issue of April 29.

January 3–May 9, 1955. Postgraduate Seminar in Psychiatry and Neurology. Page 452, issue of September 9.

January 10–15. Course in Care of Atomic Casualties. Page 285, issue of August 12.

Calendar for the Week Beginning Thursday, November 18

Thursday, November 18

*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.

*8:45–9:45 a.m. Cardiac Grand Rounds. Yamins A, Beth Israel Hospital.

*9:00–10:00 a.m. Surgical Rounds. Sherman Auditorium, Beth Israel Hospital.

*9:00–10:00 a.m. Arthritis Grand Rounds. Robert Breck Brigham Hospital.

*10:00–11:00 a.m. Combined Medical-Surgical Rounds. 5th floor teaching unit, Beth Israel Hospital.

10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by a Member of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.

*11:00 a.m. Thoracic Conference. The Treatment of Severe Chronic Bronchial Asthma. Dr. Maurice S. Segal. Main Amphitheater, Peter Bent Brigham Hospital.

*11:00 a.m.–12:00 m. Pediatric Conference. Mount Auburn Hospital, Cambridge.

*11:00 a.m.–12:00 m. Medical Staff Conference. Sherman Auditorium, Beth Israel Hospital.

*11:00 a.m.–12:30 p.m. Hand Clinic (Physical Medicine and Rehabilitation Service). Boston City Hospital.

*12:00 m.–1:00 p.m. Intravenous Fat and Parenteral Nutrition. Dr. William R. Waddell. Stearns Auditorium, New England Center Hospital.

*12:00 m.–1:00 p.m. Surgical Staff Conference. Sherman Auditorium, Beth Israel Hospital.

*12:00 m.–1:30 p.m. Teaching Conference. Diabetes in Pregnancy. Dr. David Hurwitz. New Cheever Amphitheater, Boston City Hospital.

*4:00–5:00 p.m. Pediatric Seminar. Burnham Memorial Hospital for Children (Burnham 4), Massachusetts General Hospital.

*5:00 p.m. Nu Sigma Nu. A Progress Report on an Experiment in Medical Education. Auditorium, Jimmy Fund Building, 35 Binney Street.

Friday, November 19

*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.

*9:30–11:30 a.m. Medical and Surgical Grand Rounds. Drs. George W. Thorn and Francis D. Moore. Main Amphitheater, Peter Bent Brigham Hospital.

*10:00 a.m. Tuberculosis Surgical Clinic. South End Health Unit, 57 East Concord Street.

10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by a Member of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.

*11:00 a.m. Cesarean Section Meeting. Dr. Edward Devlin. St. Margaret's Hospital, Dorchester.

*11:00 a.m.–1:00 p.m. Medical Grand Rounds. Drs. Proger and Staff. Stearns Auditorium, New England Center Hospital.

*1:30 p.m. Fertility and Endocrine Clinic. Free Hospital for Women, Brookline.

*1:30 p.m. Tumor Clinic. Mount Auburn Hospital, Cambridge.

*4:00–5:00 p.m. Child Psychiatry. Burnham Memorial Hospital for Children (Burnham 4), Massachusetts General Hospital.

*4:00–10:00 p.m. Alcoholism Clinic. By appointment. Washingtonian Hospital, 41 Waltham Street.

Saturday, November 20

*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.

*8:00–9:00 a.m. Anesthesia Conference. Dr Etsten. Pratt Lecture Hall, Joseph H. Pratt Diagnostic Hospital.

*8:30–10:00 a.m. Orthopedic Staff Conference. Boston City Hospital.

*9:00–10:30 a.m. Surgical Grand Rounds. Dr. Child and Staff. Stearns Auditorium, New England Center Hospital.

10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by a Member of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.

11:00 a.m.–12:00 m. Hematology Clinic. Dr. William Dameshek. Pratt Lecture Hall, Joseph H. Pratt Diagnostic Hospital.

Monday, November 22

*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.

*8:00–9:00 a.m. Medical and Surgical Clinic on Diabetic Problems. New England Deaconess Hospital.

*8:30–9:30 a.m. Clinic by Entire Surgical Staff and Anesthesia Staff. Cheever Amphitheater, Dowling Building, Boston City Hospital.

10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by a Member of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.

*12:00 m.–1:00 p.m. Medical-Pathological Conference. Pratt Lecture Hall. Joseph H. Pratt Diagnostic Hospital.

*12:15–1:15 p.m. Clinicopathological Conference. Main Amphitheater, Peter Bent Brigham Hospital.

*1:00 p.m. Alcoholism Clinic. Peter Bent Brigham Hospital.

*4:00 p.m. Clinicopathological Conference. Pathology Conference Room, Beth Israel Hospital.

*4:00–5:00 p.m. Surgical Pathology. Dr. MacMahon. Stearns Auditorium, New England Center Hospital.

*5:00 p.m. Alpha Omega Alpha Lecture. Metabolism of Hemoglobin and Bile Pigments. Dr. Irving M. London. Auditorium, Boston University School of Medicine, 80 East Concord Street.

*5:00–6:30 p.m. Anesthesia Group of the Lahey Clinic. Joslin Auditorium, New England Deaconess Hospital.

*7:00–8:00 p.m. Pathology Conference. Dr. MacMahon and Staff. Stearns Auditorium, New England Center Hospital.

Tuesday, November 23

*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.

*9:00 a.m. Geriatrics Clinic. Peter Bent Brigham Hospital.

10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by a Member of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.

*12:00 m. Pediatric Grand Rounds. Cheever Amphitheater, Dowling Building, Boston City Hospital.

*12:00 m.–1:00 p.m. Pediatric Combined Rounds. Burnham Memorial Hospital for Children (Burnham 4), Massachusetts General Hospital.

*12:00 m.–1:00 p.m. Endocrine Conference. Dr. Astwood. Stearns Auditorium, New England Center Hospital.

*12:15–1:15 p.m. X-Ray Conference. Dr. Merrill Sosman. Main Amphitheater, Peter Bent Brigham Hospital.

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